

**Information to be Considered to be Nominated as a European
Conformity Assessment Body (CAB) for Conducting Surveillance/
Post-Market and Initial/Pre-Approval Quality System (GMP) Audits**

I. INTRODUCTION

- A. This document describes the criteria for conformity assessment bodies (CABs) who wish to audit manufacturers of medical devices in the European Community under the terms of the Mutual Recognition Agreement between the US and the European Community.
- B. CABs seeking nomination to participate in confidence building exercises and designation to carry out audits to evaluate conformance with US Food and Drug Administration (US FDA) regulatory requirements for medical devices will themselves be subject to assessment audits against the criteria described in this document. Audits of CABs may be conducted by the US FDA or its appointed agent.
- C. Following designation, the CAB may expect to be monitored through surveillance audits at intervals determined by the US FDA. The US FDA and the Regulatory Authority have a duty to withdraw designation should the CAB fail to meet the criteria. However, designation would be withdrawn only after the matter was discussed with the CAB, and an opportunity was provided for the CAB to refute the audit findings.

II. DEFINITIONS

- A. For the purposes of this document, certain terms are defined.
 - 1. *Audit* means a systematic and independent examination to determine whether quality activities and related results comply with planned arrangements and whether these arrangements are implemented effectively and are suitable to achieve objectives [Source: ISO 8402 and 4.1 of the Global Harmonization Task Force Guideline for regulatory auditing of quality systems of medical device manufacturers. Final draft]
 - 2. *Auditee* means any organization to be audited for compliance with the relevant medical device regulatory requirements. [Source: 4.2 of the Global Harmonization Task Force Guideline for regulatory auditing of quality systems of medical device manufacturers. Final draft]

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 2. *Auditee* means any organization to be audited for compliance with the relevant medical device regulatory requirements. [Source: 4.2 of the Global Harmonization Task Force Guideline for regulatory auditing of quality systems of medical device manufacturers. Final draft]
 3. *Auditor* means a person with relevant experience and qualifications to perform audits or specified parts of such audits and who belongs to or is authorized by the auditing organization. [Source: 4.3 of the Global

Harmonization Task Force Guideline for regulatory auditing of quality systems of medical device manufacturers. Final draft]

4. *Component* means any raw material, substance, piece, part, software, firmware, labeling, or assembly which is intended to be included as part of the finished, packaged, and labeled device. [Source: 21 Code of Federal Regulations Section 820.3(c)]

5. The term “*device*” means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part or accessory, which is—

- (1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
- (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- (3) intended to affect the structure of any function of the body of man or other animals, and

which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. [Source: Federal Food, Drug, and Cosmetic Act P.L. 75-717 Stat.1040 (1938) Section 201 [321](h)]

6. *Establish* means define, document (in writing or electronically), and implement. [Source: 21 Code of Federal Regulations Section 820.3(k)]

7. *Finished device* means any device or accessory to any device that is suitable for use or capable of functioning, whether or not it is packaged, labeled or sterilized. [Source: 21 Code of Federal Regulations Section 820.3(l)]

8. *Manufacturer* means any person who designs, manufactures, fabricates, assembles, or processes a finished device. Manufacturer includes but is not limited to those who perform the functions of contract sterilization, installation, relabeling, remanufacturing, repacking, or specifications development. [Source: 21 Code of Federal Regulations Section 820.3(o). Note: For the purposes of this document, the part of the definition that refers to “... initial distributors of foreign entities performing these functions” has been omitted, because initial distributors of foreign entities are present only in the United States of America.]

9. *Remanufacturer* means a person who processes, conditions, renovates, repackages, restores, or does any other act to a finished device that significantly changes the finished device's performance or safety specifications, or intended use. [Source: 21 Code of Federal Regulations Section 820.3(w)]

III. SCOPE

- A. These criteria shall be used to nominate CABs to participate in confidence building activities for the purpose of assessing the ability of CABs to conduct quality system evaluations of manufacturers who:
1. are located in the member states of the European Community;
 2. manufacture medical devices regulated by both the US FDA and the European Community;
 3. and export or intend to export these medical devices to the United States of America.
- B. CABs will conduct audits of device manufacturers to evaluate the auditee's quality system and conformance to the acts, regulations, statutes, and laws which are applicable to medical devices and enforced by the US FDA.
- C. Manufacturers of components who sell or otherwise distribute said components to manufacturers who incorporate these components into finished devices shall not be subject to quality systems evaluations/audits under the terms of this agreement. Manufacturers of components of or accessories to devices, who package and label such components and/or accessories for distribution to medical facilities, shall be considered manufacturers of finished devices and shall be subject to quality system evaluations/audits under the terms of this agreement.
- D. For the purposes of this document, applicable acts, regulations, statutes and laws include:
1. The Federal Food, Drug, and Cosmetic Act, Public Law Number 75-717, 52 Stat. 1040 (1938)
 2. 21 Code of Federal Regulations Part 800 – General
 3. 21 Code of Federal Regulations Part 801 – Labeling

4. 21 Code of Federal Regulations Part 803 – Medical device reporting
5. 21 Code of Federal Regulations Part 805 – Establishment registration and device listing of manufacturers and distributors of devices
6. 21 Code of Federal Regulations Part 806 – Reports of corrections and removals
7. 21 Code of Federal Regulations Part 809 – In vitro diagnostic products for human use [when the EC determines to regulate said products as medical devices.]
8. 21 Code of Federal Regulations Part 810 – Medical device recall authority
9. 21 Code of Federal Regulations Part 812 – Investigational device exemptions
10. 21 Code of Federal Regulations Part 814 – Premarket approval of medical devices
11. 21 Code of Federal Regulations Part 820 – Quality system regulation
12. 21 Code of Federal Regulations Part 821 – Medical device tracking requirements
13. 21 Code of Federal Regulations Part 860 – Medical device classification procedures
14. 21 Code of Federal Regulations Parts 862-892
15. 21 Code of Federal Regulations Part 895 – Banned devices
16. 21 Code of Federal Regulations Part 1002 – Records and reports
17. 21 Code of Federal Regulations Part 1004 – Repurchase, repairs, or replacement of electronic products
18. 21 Code of Federal Regulations Part 1005 – Importation of electronic products
19. 21 Code of Federal Regulations Part 1010 – Performance standards for electronic products: general
20. 21 Code of Federal Regulations Part 1020 – Performance standards for ionizing radiation emitting products

21. 21 Code of Federal Regulations Part 1030 – Performance standards for microwave and radio frequency emitting products
22. 21 Code of Federal Regulations Part 1040 – Performance standards for light-emitting products
23. 21 Code of Federal Regulations Part 1050 – Performance standards for sonic, infrasonic, and ultrasonic radiation-emitting products

IV. GENERAL

REQUIREMENTS

- A. **Resources:** The CAB shall provide the resources for conformity assessment of manufacturers of medical devices in regard to the US FDA laws and regulations for medical devices, the Food, Drug and Cosmetic Act and 21 Code of Federal Regulations Parts 800 through 1050, in a competent, transparent, neutral, independent and impartial manner.
- B. **Legal Status:** The CAB shall be a legally defined entity and shall make available to the Regulatory Authority or its appointed agent or the US FDA or its appointed agent on request:
 1. documentation clearly identifying its legal status;
 2. a description of the means by which the CAB obtains financial support;
 3. documentation which clearly shows both the authority and the responsibility of individuals within, and the reporting structure of, the CAB.
- C. **Language:** Documentation described above which is submitted to the US Food and Drug Administration is expected to be in English.
- D. **Organizational structures:** If the CAB is a legal entity which is part of a larger organization, the links and relationship between the CAB and the larger organization shall be clearly documented.
- E. **Subcontracting:** Where the CAB uses the services of a subcontractor, the CAB is responsible for all contracted actions of its subcontractor and shall be liable for them as if the CAB itself performed the actions.

V. INDEPENDENCE

FDA will expect CABs to be impartial and free from any commercial, financial, and other pressures that might present a conflict of interest or an appearance of conflict of interest. FDA believes the CAB should have established, documented, and executed policies and procedures to prevent any individual or organizational conflict of interest. Although it is not feasible to identify all of the circumstances that would raise concerns about conflicts of interest, the most common conditions that would indicate a potential conflict of interest are:

- a) the CAB is owned, operated, or controlled by a device manufacturer or distributor;
- b) the CAB or any of its personnel involved in 510(k) evaluations or quality system evaluations has an ownership or other financial interest in any medical device, device manufacturer, or distributor;
- c) the CAB or any of its personnel involved in 510(k) evaluations or quality system evaluations participates in the design, manufacture, or distribution of any medical device;
- d) the CAB or any of its personnel involved in 510(k) evaluations or quality system evaluations provides consultative services to any device manufacturer or distributor regarding any specific devices;
- e) the CAB or any of its personnel involved in 510(k) evaluations or quality system evaluations participates in the preparation of any 510(k) and/or quality system consultation;
- f) the fee charged or accepted by the CAB is contingent or based upon the type of recommendation made; or
- g) the CAB uses in the evaluation of a 510(k) or in the quality system evaluation, personnel who were employed within the last twelve months by the firm who submitted the 510k for evaluation or requested a quality system evaluation.

A CAB may assess a fee for its services and conduct other activities, such as objective testing of devices, if the services and activities do not affect the impartiality of 510(k) evaluations or quality system evaluations.

Where a CAB uses the services of a contractor, the CAB is responsible for the contracted work. The CAB is to assure that the contractor meets the CABs established criteria for freedom from conflicts of interest.

Information on the conflict of interest standards FDA applies to its personnel is included in Appendix B to this document, "Standards of Ethical Conduct for Employees of the Executive Branch". A CAB may adopt these standards as one means of safeguarding its operations against conflicts of interest.

VII. TECHNICAL COMPETENCE

REQUIREMENTS

- A. Knowledge & training: CAB personnel shall possess satisfactory knowledge of the US FDA laws and regulations for medical devices for the audits they perform and shall have adequate experience in their area of competence. Personnel involved in the assessment of conformance with US FDA regulatory requirements for medical devices shall have received training in accordance with training requirements described in this section and Appendix 2.
- B. Records: Records shall be available to demonstrate that personnel have the appropriate experience and have received appropriate training relevant to the CAB's auditing activities.
- C. Auditor's experience: CABs carrying out audits of quality systems of medical device manufacturers shall require that such quality system audits are conducted by an auditor who is experienced in the evaluation of quality systems and the technologies used by the manufacturer or a team that includes at least one member who is experienced in the evaluation of the technologies used by the manufacturer.

GUIDANCE

- a. The management of the CAB should satisfy themselves that personnel who administer and perform audits are competent to fulfill the tasks required of them.
- b. One or more members of an assessment team should be trained and/or experienced in each of the following skills that is relevant to the assessment being made:
 - 1. the production methods and the test and verification procedures applicable to the various types of medical devices subject to the audit,
 - 2. the assessment of design documentation to determine that all aspects of the design control and development activity are in compliance with the requirements of the Quality System Regulation, 21 Code of Federal Regulations Section 820.30;
 - 3. for sterile medical devices, microbiological assessment, including environmental control, and validation and routine control of sterilization processes; and
 - 4. the assessment and evaluation of quality systems.

- c. Competence must be present within the audit team as a whole but not necessarily by each member of it. In assessing conformance of manufacturers with applicable US FDA regulatory requirements for medical devices, the audit team may include additional experts in processes and technologies relevant to the scope of the audit. Ideally these experts should meet the qualifications described in VII.d. The experts authorized by the auditing organization, who are not qualified as auditors, should assess only those processes related to their specialized knowledge and under the supervision of an auditor. Alternatively, the members of the audit team may be given additional training and/or specialized knowledge related to those processes and technologies.
- d. Personnel involved in auditing quality systems should be qualified in accordance with ISO 10011-2 or its equivalent, and should be capable of functioning in accordance with the relevant parts of ISO 10011-1 or its equivalent. The management of quality systems assessments should be in accordance with ISO 10011-3 or its equivalent.
- e. For each auditor, a record should include the following information:
 - 1. name of auditor;
 - 2. designated areas of competence and responsibility;
 - 3. educational and professional qualifications;
 - 4. work experience (relevant to the activities being performed);
 - 5. details of training received relating to assessment activities, including training in the US FDA laws and regulations for medical devices identified in the Scope, and relevant standards, policies, and procedures.

VIII. RESOURCES

REQUIREMENTS

- A. Extent: The CAB shall have available the appropriate resources to enable auditors to carry out audits effectively.

GUIDANCE

- a. The buildings and resources should enable the CAB to perform the technical and administrative tasks connected with evaluation and verification.

IX. CONFIDENTIALITY

REQUIREMENTS

- A. Non-disclosure: The CAB shall ensure confidentiality of any information obtained in the course of conducting audits under the MRA.
- B. Authorized disclosure: The CAB shall ensure that no details, records, results, or information of any kind are disclosed to any other party except the Regulatory Authority, the US FDA, and the auditee.
- C. Audit reports: The results of audits shall be provided to the US FDA in the form of preliminary reports as necessary and abbreviated reports or complete reports where appropriate. Preliminary reports are necessary when devices that have been correctly put into service and used in accordance with their intended use have been found to compromise the health and/or safety of patients or users. Complete reports shall be provided during the confidence building period. Abbreviated reports shall be provided after the confidence building period has been concluded and CABs are designated to fully participate in auditing under the terms of the MRA. Following the designation of CABs, complete reports shall be supplied to the US FDA upon request. All reports are expected to be in English and to be typed.

GUIDANCE

- a. Documented procedures should describe the means by which the CAB maintains confidentiality between itself and its clients. Procedures should describe the mechanism through which CAB personnel are made aware of confidentiality requirements. For example, staff may be required to sign a declaration not to divulge any information gained about clients to third parties.
- b. Subclause IX.A. does not apply to communication of information relating to the issuance, refusal, or withdrawal of certificates by CABs to the Regulatory Authority, other CABs or the US Food and Drug Administration.

X. SUBCONTRACTORS

REQUIREMENTS

- A. **Contract Requirements:** Where tasks relating to conformity assessment are carried out on behalf of a CAB by external subcontract organizations or individuals, the CAB shall ensure that these subcontractors and their personnel conform to all the requirements of these criteria that would apply as if the task had been performed by its own personnel.
- B. **Limitation to scope:** The CAB shall not subcontract the overall responsibility for reviewing the results of audits, which are the essential tasks for which it was nominated and/or designated. Subcontractors shall fulfill only an objective role, which is restricted to factual reporting and/or supported recommendations on the basis of which the CAB shall make assessments and judgments in relation to the requirements of the regulations.
- C. **Supervisory control:** The CAB may subcontract to an individual or organization those parts of audits that require specialized knowledge and/or are limited in scope. In such situations, the CAB shall provide supervisory control over the subcontractor by a CAB auditor. The CAB may subcontract the entire inspection to an individual or organization. In such situations the CAB shall abide by subclause X.B. in making the final assessment and judgment regarding whether the auditee meets the requirements of the regulations.
- D. **Documented agreement:** A documented agreement shall be drawn up between the CAB and the subcontractor reflecting these requirements, including confidentiality and the provision of access for the US FDA and/or its designated agent. The documented agreement shall include a requirement that the subcontractor certify conformance with the conflict of interest requirements described in Appendix A. This agreement shall also prohibit subcontractors from further subcontracting their duties.
- E. **Subcontractor's procedures:** The CAB shall ensure that the subcontracted activities are carried out according to detailed documented procedures which are the same as, or judged by the CAB to be equivalent to, those followed by the CAB itself when auditing for conformance with US FDA laws and regulations for medical devices.
- F. **Documentation:** The CAB shall keep an up to date register of all its subcontractors, which shall be provided to the US FDA or its designated agent without delay on request. The CAB shall maintain documentary evidence that the subcontractor has the necessary technical competence and resources to carry out the subcontracted activities.

GUIDANCE

- a. A CAB which subcontracts duties remains in all cases responsible for all activities conducted by the subcontractor on behalf of the CAB. Subcontracting does not entail the delegation of powers or responsibilities.
- b. The subcontractor register maintained by the CAB should include the following information:
 1. the name of the subcontractor and/or the subcontract organization;
 2. its legal status and details of any relationship with a parent company, group of companies, or any other organization of which the subcontractor is a part or has an ongoing business relationship;
 3. names of staff members carrying out the subcontracted activities and evidence that they are competent to do so;
 4. the precise duty performed by the subcontractor (e.g. software validation assessment, etc.); and
 5. details of the procedures used in carrying out the subcontracted duties.
- c. A CAB which subcontracts duties should document the means by which it ensures that the conflict of interest requirements and confidentiality requirements are made known to subcontractors.
- d. The conditions of this clause apply to any subcontractor whether or not it is located on European Community territory. Subcontractors are not necessarily resident in the European Community, but their activities are defined by contract, which is interpreted by applicable law of the member state in which the CAB is located.

XI. QUALITY SYSTEM

REQUIREMENTS

- A. Documentation: The CAB shall establish and maintain procedures and records, which together demonstrate its compliance with the Mutual Recognition Agreement and this document. As appropriate, this documentation shall include the following:

1. a description of the legal status of the CAB, including the links and relationship with parent organizations, if relevant;
2. documentation showing the responsibilities and reporting structure of the CAB;
3. the scope of the responsibilities for each auditor;
4. the names of auditors, their responsibilities in regard to auditing, and records of their relevant training and experience;
5. a description of the process by which manufacturers can request that the CAB audit their conformance with US FDA requirements for medical devices;
6. Procedures detailing the rationale for fixing time limits for completion of evaluation and verification activities conducted during the audit;
7. Records to support the evaluation, assessment, and conclusions about the manufacturer's compliance with the requirements of the US FDA for medical devices;
8. Procedures describing the means by which auditing and consulting services and staff are separated, whether these services are carried out by the CAB or any part of a larger organization to which it is linked, or its subcontractors; and
9. Details of record keeping facilities including means to ensure security and confidentiality.

A system shall be maintained to control all quality system documentation and to ensure that current issues of procedures are available at all relevant locations.

- B. Implementation: The CAB shall ensure that the defined quality system procedures are implemented effectively.
- C. CABs shall have appropriate resources for conducting quality systems audits on manufacturers' premises

APPENDIX A: CONFLICT OF INTEREST AND REPORTING REQUIREMENTS

See Information on Conflict of Interest Standards for FDA Reviewers and Standards of Ethical conduct for Employees of the Executive Branch.

APPENDIX B: AUDITOR QUALIFICATIONS AND TRAINING REQUIREMENTS

AUDITOR QUALIFICATIONS

- A. Education: The educational requirements for auditors consist of a bachelor's degree from a four year college or university in one of the fields listed below or a degree from a two year program at a technical institution in one of the fields listed below:
1. biology or microbiology
 2. chemistry or biochemistry
 3. computer and software technology
 4. electrical, mechanical, or bioengineering
 5. human physiology
 6. medicine
 7. pharmacy
 8. physics or biophysics
- B. Knowledge, skills, and abilities: Auditors should possess the knowledge, skills, and abilities to enable them to effectively audit for conformance with US FDA regulatory requirements for medical devices. Auditors should:
1. have knowledge of existing US FDA policies, regulations, and procedures for conducting audits for conformance with US FDA regulatory requirements for medical devices and the ability to apply these policies, regulations, and procedures during the audit;
 2. be able to evaluate the state of control of the auditee's quality system;
 3. be able to evaluate the auditee's conformance with the US FDA's regulatory requirements for medical devices;
 4. be able to recognize, collect, and identify appropriate evidence of nonconformities to support assessments and evaluations of the auditee's level of conformance with US FDA regulatory requirements;

5. be able to communicate verbally so as to clearly explain the auditee the purpose and scope of the audit and any nonconformities identified and respond appropriately to questions asked by the auditee; and
6. be able to document the findings of the audit in English in writing in accordance with a report format specified by the US FDA.

B. Training. Training should facilitate the development of the knowledge, skills, and abilities described above. The following are the requirements for training in addition to those described in Section VI. Technical Competence:

1. US FDA regulatory requirements for medical devices;
2. US FDA policies and procedures for auditing manufacturers of medical devices including applicable compliance programs, and those sections of the Investigations Operations Manual, Compliance Policy guides, and Regulatory Procedures Manual that are applicable to audits in general and medical devices specifically;
3. auditing principles;
4. evidence development;
5. investigative interviewing;
6. design control; and
7. process validation.