



# **The APIC Audit Programme Version 6, September 2019**

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## 1 General

According to the EU legislation '*the holder of a manufacturing authorization shall at least be obliged to comply with the principles and guidelines of good manufacturing practice for medicinal products and to use as starting materials only active substances, which have been manufactured in accordance with the detailed guidelines on good manufacturing practice for starting materials*' (Directive 2001/83/EC as amended, article 46(f) for Human Medicinal Products and Directive 2001/82/EC, Article 50(f) for Veterinary Medicinal Products).

The Document entitled "Guidance on the occasions when it is appropriate for Competent Authorities to conduct inspections at the premises of manufacturers of active substances used as starting materials" (1) and the EMA Website GMP Question and Answers on audits of active substances manufacturers ([http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q\\_and\\_a/q\\_and\\_a\\_detail\\_00027.jsp&mid=WC0b01ac05800296ca](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_00027.jsp&mid=WC0b01ac05800296ca)) give further guidance on what the European Authorities expect in terms of assessing the GMP status of active substance, intermediates, starting materials (SM) and critical raw materials (RM) manufacturers.

An audit conducted by or done on behalf of the Manufacturing Authorisation Holder (MAH) of their Active Pharmaceutical Ingredient (API) Manufacturers/Suppliers should be an integral part of the Supplier Qualification Procedure of the MAH.

API manufacturers need to have a risk based approach for auditing critical RM, SM, and filed intermediates in their supplier qualification programme as required by the Falsified Medicine Directive (FMD) 2011/62/EC.

Audits should be performed by qualified and trained staff, the audit should be properly documented and the audit reports will be subject to inspection by the Competent Authorities during inspections of the MAH for the Medicinal Products and API manufacturers.

Audits should be done periodically using a risk based approach to assess the continuing cGMP Compliance status of the API, intermediates, critical RM and SM Manufacturers and, as necessary, the Agent, Broker, Packer, Re-Packer, Distributor or Importer.

If a Third Party is involved during auditing then the MAH or API manufacturer as "contract giver" should follow Chapter 7 of the EU GMP Guide and evaluate the auditors/audit process of the Third Party as the "contract acceptor" to ensure that the audit process complies with their cGMP expectations. The MAH and API manufacturer should ensure there is no conflict of interest between the audit process, the auditors and the Auditee. In view of the legal background and the cGMP expectation of supplier evaluation by the authorities, the Qualified Person(s) or responsible person(s) of the MAH and/or API manufacturer is responsible to assure that the materials used in Human and Veterinary Medicinal Product Manufacture are manufactured according to the EU GMP guidelines for APIs.

Several Audit Options are acceptable to the European Authorities:

- The Customer/Supplier Audit or **Second Party Audit** that would be performed by the Qualified Auditors of the MAH and /or API manufacturer for each material used in API manufacturing. The audit may also be performed by the Qualified Auditors of the MAH, for example in the case where the Marketing Authorisation Holder is responsible for the Manufacture or Supply of the API and contracts out the manufacture of the Medicinal Product to the MAH for the Medicinal Product.

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(1) The Guidance was published in 'Compilation of Community Procedures on Inspections and Exchange of Information', [http://ec.europa.eu/health/files/eudralex/vol-10/2013\\_ema385898\\_rev\\_16.pdf](http://ec.europa.eu/health/files/eudralex/vol-10/2013_ema385898_rev_16.pdf) and [http://ec.europa.eu/health/files/pharmacos/docs/doc2005/03\\_05/asm\\_inspections\\_guidance\\_final\\_20050303\\_en.pdf](http://ec.europa.eu/health/files/pharmacos/docs/doc2005/03_05/asm_inspections_guidance_final_20050303_en.pdf)

The Second Party Audit can also be applied to outsourced or contracted material manufacturing and performed by qualified auditors of the MAH and/or API manufacturers

The audit report and findings should be reviewed by the Qualified Person(s) of the MAH or the responsible person of the API manufacturer. In this case, the responsibilities for auditing of the material Manufacturer should be defined in the Technical Contract.

- A **Third Party Audit** of the material Manufacturer performed on behalf of the Qualified Person(s) or responsible person(s) of the MAH and/or API manufacturer. The Qualified Person(s) or responsible person(s) of the MAH and/or API manufacturer (Contract Giver) confirms that the Third Party Audit Process provides an effective assessment of the cGMP status of the material manufacturer and that the audit is performed by independent, qualified Auditors with no conflict of interest.
- **Shared Third Party Audits** are acceptable to the European Authorities as long as the Qualified Person(s) and /or responsible persons in API manufacturing ensures that the scope of the audit is applicable to each material used in API manufacturing or Medicinal Product.

A Third Party Audit can either be initiated by one or more Manufacturing Authorisation Holder(s) ('called 'customer') or by the API Manufacturer / Distributor / Broker / Importer/ Packer / Re-Packer itself (called 'Auditee').

If the API Manufacturer / Distributor / Broker/ Importer/ Packer / Re-Packer initiates the audit, the purpose of the audit is a **self-assessment** of the cGMP status of the API Manufacturer.

A Third Party Audit for critical RM, SM and intermediates can be applied to qualify the cGMP status of the manufacturer

The API manufacturers may use such audit programmes beyond the EU QP requirements as part of their own material supplier qualification management. Guidance on Supplier Qualification and Management is given in the APIC publication

- The customer of the Third Party Audit should decide for themselves whether there are any conflict of interest issues with any Third Party Audit Option.

## 2 APIC Audit Programme

The approach taken by many Medicinal Product and API Manufacturers towards this legal requirement is to perform one to one audits of their material manufacturers. However it is recognized that audits are time-consuming and expensive for both the API and Medicinal Product Manufacturer and there is potential for significant audit overload for the Pharmaceutical and chemical Industry if this is the only option used.

The aim of the APIC Audit Programme is to provide a standardised Third Party Auditing process to ensure that an effective assessment is performed of the cGMP status of critical RM, SM, intermediates and APIs; These APIs are used as Starting Materials for Medicinal Products and in so doing contribute to the assurance of the Quality, Safety and Efficacy of the Medicinal Products.

The API Compliance Institute as a Business Unit of Concept Heidelberg has been contracted by APIC to administer the APIC Audit Programme.

The audits within the framework of the APIC Audit Programme are conducted by APIC Certified Auditors and standardised reports with classification of findings are issued.

Third Party Audits for APIs should be initiated by the Marketing Authorisation Holder for the Medicinal product according to the European directive 2001/83/EC and its amendments where it is defined that it is the responsibility of the MAH to assure that the API is manufactured in accordance with the cGMPs in force.

Third Party Audits related to critical RM, SM and intermediates can be performed on request against the applicable parts of ICH Q7.

In the case that several MAHs and/or API manufacturers wish to cooperate on an audit of the same material Manufacturer or share an audit report the 'Third party audit' becomes a '**Shared Third Party Audit**'. Once the initial request to arrange the audit has been made to The API Compliance Institute, other potential customers for the 3<sup>rd</sup> Party Audit could be contacted using the standardised letter (Annex 4) and if they wish to share this audit, they should contact the API Compliance Institute 4 weeks at latest before the audit takes place.

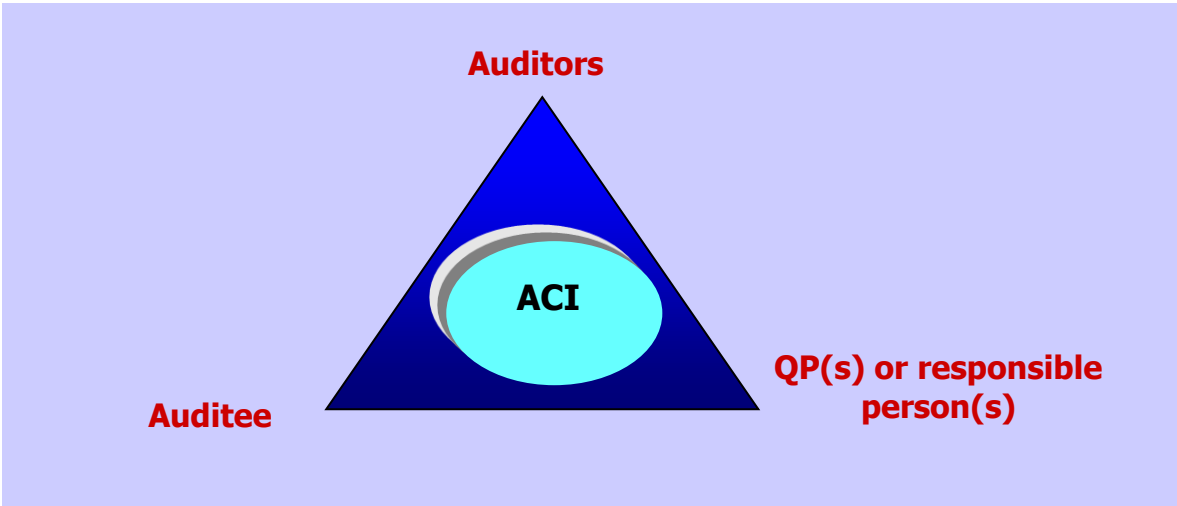
In the case that a Third Party Audit has recently been performed and the Manufacturer is contacted by a QP or responsible person of another MAH and/or API manufacturer who is interested in assessing whether this Third Party Audit Report satisfies his requirements, the representative of the MAH and/or API manufacturer should be asked to contact the API Compliance Institute. This scheme can also be applied to non EU MAH and/or API manufacturers.

In the case that the material Manufacturer/Distributor/Broker/Importer/Packer/Re-Packer initiates the request for a Third Party audit of their Manufacturing Site, the audit will be for the purpose of performing a **self-assessment audit**. This will be documented in the Audit Agreement and included as a Footnote in the Audit Report.

**Important:**

The 'Compliance Triangle principle' (see figure 1) will be followed at all steps of the audit process to ensure that all parties involved - the 'customer', the 'Auditee', the auditors and the API Compliance Institute as the coordinator of the audit are involved in the communication processes.

**Figure 1: Compliance Triangle Principle of the APIC Third Party Audit Programme**



**Request by the QP(s) or Responsible Person(s) of the Manufacturing Authorisation Holder(s): Third Party Audit of API Starting Material used in Medicinal Products and critical RM, SM, filed intermediates, excipients.**

**Request by the API Manufacturer/Distributor/Broker/Importer/Packer/Re-Packer: Self Assessment Audit of GMP status**

**ACI = API Compliance Institute**

**Auditee = Manufacturer/Distributor/Broker/Importer/Packer/Re-Packer**

**QP = Qualified Person or responsible person**

Participation in the APIC Audit Programme is on a voluntary basis and is not limited to members of APIC or to a specific region of the world.

The CEFIC APIC Auditing Guide documentation

([http://apic.cefic.org/pub/Auditing/APIC\\_CEFIC\\_AuditingGuideAugust2016.pdf](http://apic.cefic.org/pub/Auditing/APIC_CEFIC_AuditingGuideAugust2016.pdf)) provides the framework for the standardised audit programme. Trained Auditors follow the principles defined in the Auditing Guide, to ensure that a comprehensive assessment of the cGMP status of each Manufacturer or as necessary Distributor, Trader, Broker, Importer, Packager, Re-packager of the Material is performed and that full documentation is available to describe the audit.

The audit report will include descriptions of all items covered during the audit. Objective evidence for any cGMP deficiencies found during the audit will be included in the report and such deficiencies will be categorized by the Auditors in one of the following categories (classification rating see Q&A EU GMP guide part II: Basic requirements for active substances used as starting materials: GMP compliance for active substances

[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q\\_and\\_a/q\\_and\\_a\\_detail\\_000027.jsp](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000027.jsp)).

**Critical Deficiency:**

A deficiency which has produced, or leads to a significant risk of producing an Active Pharmaceutical Ingredient that could be harmful to the human or veterinary patient.

The condition violates essential cGMP-rules and/or essential quality assurance practices.

**Major Deficiency:**

A non critical deficiency which has produced or may produce a product, which does not comply with its marketing authorization or which indicates a “major” deviation from cGMP, or a combination of several “other” deficiencies, none of which on their own may be major, but which may together represent a major deficiency and should be explained and reported as such.

**Other Deficiency:**

A deficiency, which cannot be classified as either critical or major, but which indicates a departure from cGMP.

(A deficiency may be “other” either because it is judged as “minor”, or because there is insufficient information to classify it as a major or critical).

### **3 The Auditors**

#### **3.1. Educational Background and Experience**

The Auditors should have a good educational knowledge of chemistry. Qualifications as Pharmacist, Medical Doctor, Chemical Engineer, graduate or Ph.D. in Chemistry, Biology or related fields as Agrochemistry etc., are appropriate. A good understanding of biochemistry and analytical techniques and practices is a definite advantage.

At least 5 years practical experience of cGMP manufacture of Active Pharmaceutical Ingredients may also be considered as sufficient knowledge and background.

Auditors should be aware of and understand the changes and implications of regulatory requirements in API manufacturing. This knowledge is usually obtained through training and experience.

#### **3.2 Auditor Training Courses for ‘Certification’**

Attendance at a specific five-day training course sponsored by APIC (two and a half days related to cGMPs in API manufacture and two and a half days for training in effective auditing techniques) is a prerequisite for becoming an APIC Certified Auditor. The participant will receive a certificate of attendance for each of the two training courses.

The seminar fees will be charged directly to the Auditor or his company.

##### **3.2.1 Certification of Auditors**

In the APIC Audit programme 3 possibilities are given:

- Certificate of Attendance: The participant of the specific five-day training will receive a certificate of attendance for each of the two training courses.
- APIC Certified Auditor: In order to become an APIC Certified Auditor, the Auditor has to undergo an assessment and 2 written examinations. The first exam is about general GMP topics and takes place directly after the Auditor Training Course. The second exam is an internet based test approx.. 2 weeks after the Auditor Training Course is finished and consists of a total of 30 questions. These have to be answered following the multiple-choice procedure. For this task, the participant has 60 minutes. He/she has passed the exam if 80% of the questions have been answered correctly. In case of failure, the exam can be repeated twice. The costs have to be borne by the participant.
- During the Auditor Training Course an APIC representative who is a trainer in the course and a trainer with academic education in psychology assess the auditing skills of the participants. The APIC representative judges the participant's ability to conduct audits according to the provisions of the APIC Auditing Programme. The psychologist assesses the verbal and non-verbal communication, analyses the art of questioning and conversation techniques as well as the behavior in conflict situations. These ratings are put down on a form including a statement whether or not the trainee auditor should become an

APIC Certified Auditor and the form is archived at the API Compliance Institute together with the record of performance in the examination.

Auditors who have successfully passed the examinations and the assessment will then become APIC Certified Auditors. The Certificate is valid for three years.

The API Compliance Institute keeps a register of all APIC Certified Auditors.

On request by the certified APIC auditor his/her certification can be extended provided he/she can show evidence that he/she

- has attended at least two training courses / conferences on current GMP topics
- has performed at least three audits

during the current period of his/her certification.

The ACI decides on requalification of the auditor. In case of doubt an APIC representative should confirm in writing that he agrees with the recertification.

If these conditions are not met or the request for re-certification was not made by the certified APIC Auditor, his/her name will be withdrawn from the register of APIC Certified Auditors by the ACI.

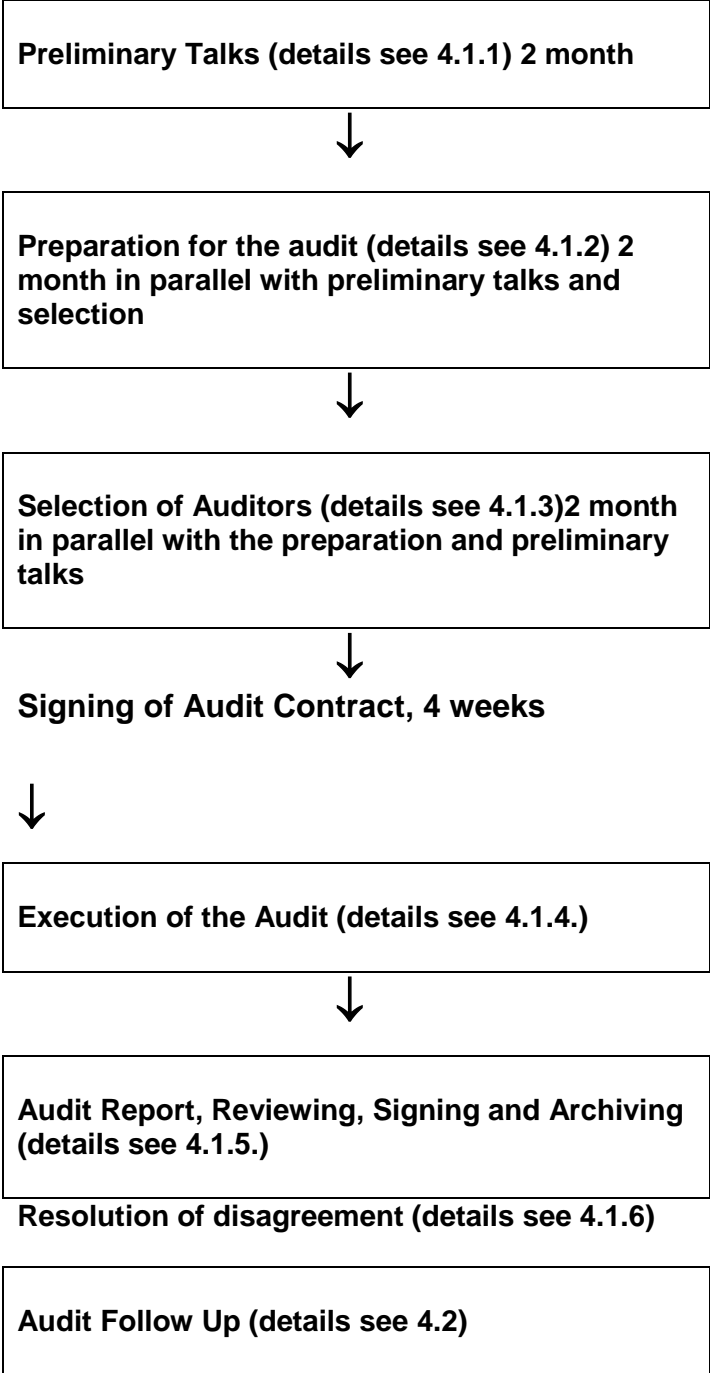
### **3.3 Contract**

'APIC Certified Auditors' who agree to conduct audits in the framework of the APIC Audit Programme have to sign a contract with the API Compliance Institute (see Annex 1). This contract lays down the obligations of the Certified Auditor.

**4 The Audit Process**

**4.1 Steps of the Audit Process**

The following section describes the steps that should be followed in the audit process from the initial contact with the API Compliance Institute by the potential customer until the distribution of the audit report. The timings mentioned below are maximum time frames however the timeframes can be reduced to support urgent requests





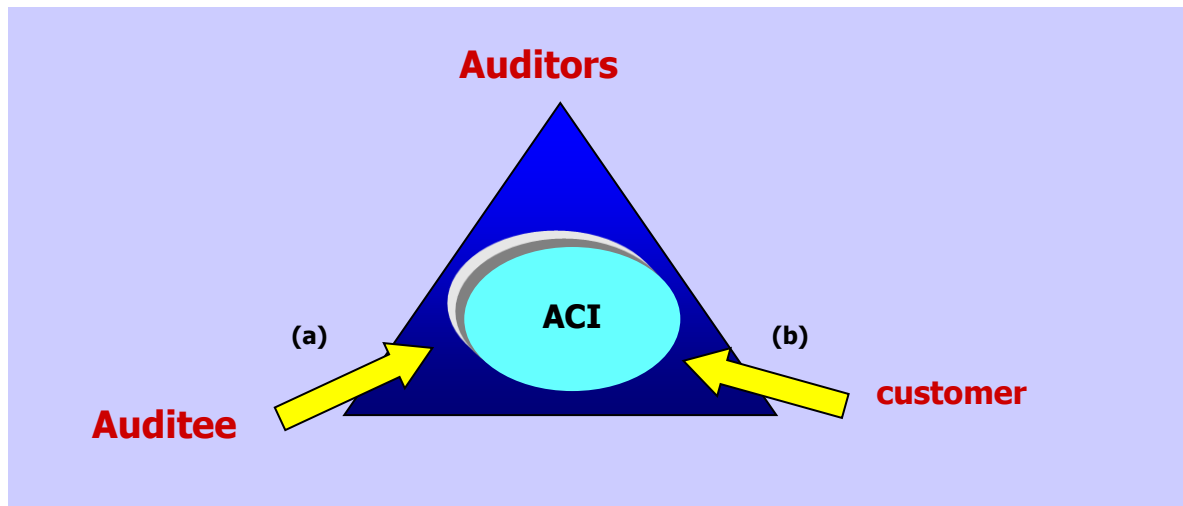
#### 4.1.1 Preliminary Talks

A Third Party Audit should be initiated by one or more QP(s) and/or responsible person(s) of MAH(s) and/or API manufacturer(s) ('called 'customer').

Requests to initiate Third Party Audits should be made to the API Compliance Institute in all cases.

Audit requests will follow the Compliance Triangle Principle (see Figure 2).

**Figure 2: Compliance Triangle Principle of the APIC Third Party Audit Programme, Preliminary Talks**



**(a) Request by the Auditee: self assessment of cGMP status**

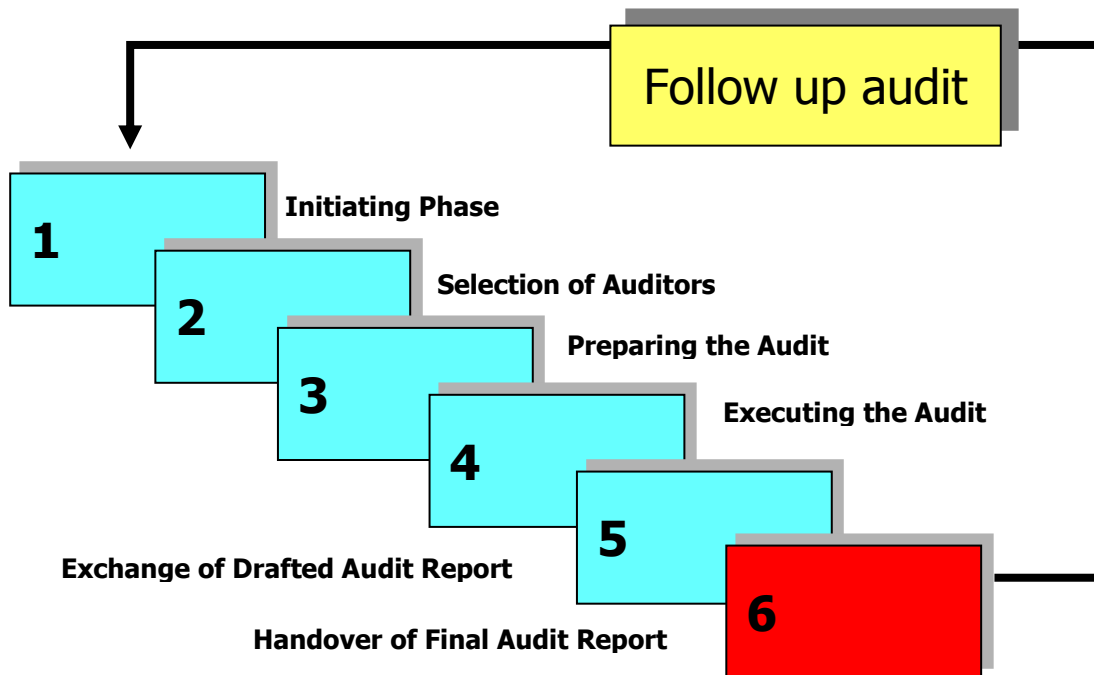
**(b) Request by customer: Third Party Audit of critical RM, SM, intermediates and APIs**

Before formal placement of an order by the customer, the API Compliance Institute will have preliminary talks on the following topics, among others:

- Provide details of the objectives and structure of the APIC Audit Programme so that the customer can verify that the audit process is suitable with respect to Chapter 7 of EU GMP Guide relating to Contract Services.
- Scope of the audit
- Steps of the audit process
- Expected time inputs and expected costs
- Timetable, if desired
- Discuss potential involvement of other customers with the material Manufacturer and initial customer requesting audit to encourage Shared Third Party Audit Option.
- Standardised letters (Annex 4) to encourage The Shared Third Party Audit Options will be sent by the ACI to the customers and Auditee to explain the Shared Third Party Audit Option and if they are in agreement, the relevant Standardised Letters may then be sent to other customers who may be interested in participating in the Shared Third Party Audit.

The following standardised approach will be followed.

**Figure 3: Standardised Audit Process**



If the customer is interested in ordering an audit, the API Compliance Institute will send the necessary documents, including the Audit Agreement ([see Annex 2](#)) to the customer. The customer can define any specific points that should be covered in the audit for example corrective actions from previous audits in the amendment to the Agreement.

The Audit Agreement has to be signed by all parties involved, the customer, the Auditee, the auditors and the API Compliance Institute. When more than one QP or Responsible Person(s) of the MAH(s) and/or API manufacturer(s) are requesting the audit, for reasons of confidentiality, contracts with each QP or responsible person can be documented separately.

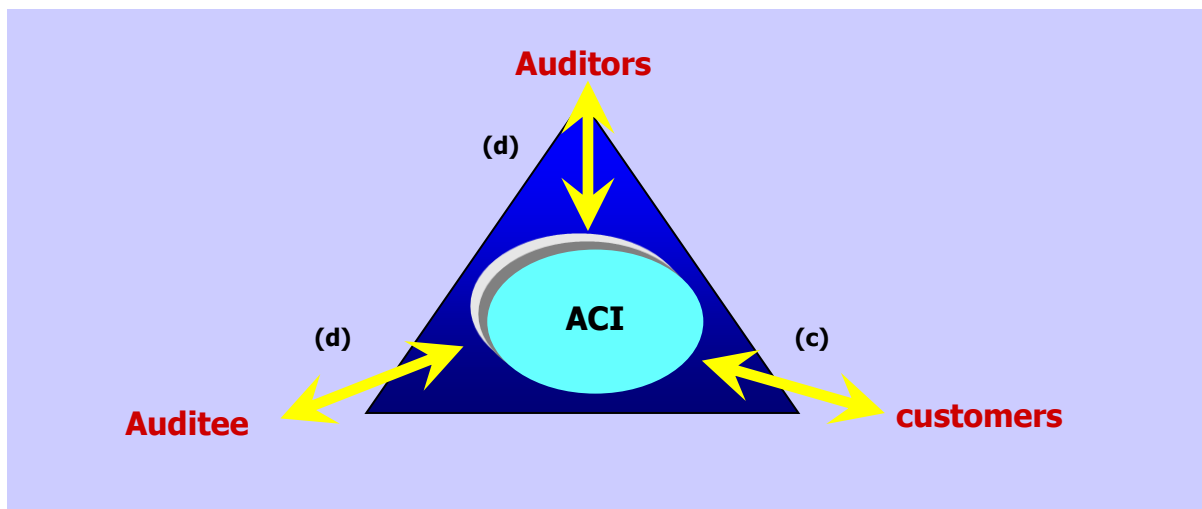
In case of a 'self-assessment audit', the Audit Agreement has only to be signed by the customer as Auditee, the auditors and the API Compliance Institute.

The services listed in the following sections on the individual steps of the audit take place after the Audit Agreement has been signed by all parties and returned to the API Compliance Institute.

A Secrecy Agreement that is designed to protect the confidential information of the Auditee will be prepared and signed. A proposed Secrecy Agreement is available in [Annex 3](#).

#### 4.1.2 Preparation for the Audit

**Figure 4: Step (1): Initiating Phase**



**(c) customers contact(s) ACI**

**(d) ACI contacts the Auditee and sends the pre-audit questionnaire and contacts the required number of suitable APIC certified auditors**

For gaining initial information about the Auditee and to effectively plan the audit a pre-audit questionnaire (for further details see Appendix B of APIC Auditing Guide) will be sent by the API Compliance Institute to the Auditee in advance.

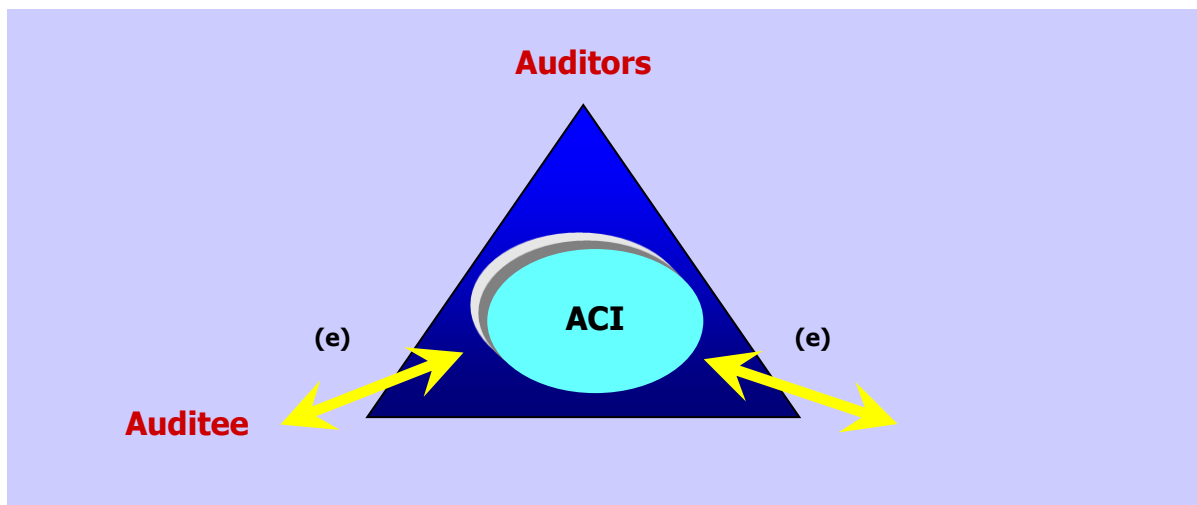
After return of the completed questionnaire, the required number of suitable auditors will be selected by the API Compliance Institute according to section 3.1.3 based on the information given in the questionnaire.

The questionnaire will also be forwarded to the selected auditors for their preparation. If, after evaluation of the questionnaire, the auditors will have any doubt of a successful audit, the Auditee will be contacted by the API Compliance Institute to discuss on how to proceed.

The Auditee will appoint a contact person (audit representative) responsible for the handling of the audit.

### 4.1.3 Selection of Auditors

Figure 5: Step (2): Selection of Auditors



- (e) **ACI informs the Auditee and the customers about the names of the chosen APIC certified auditors. Both the Auditee and/or the customers can refuse one or both auditors (e.g. due to competition reasons)**

In general, for API auditing the API Compliance Institute will select two Certified Auditors from the APIC register. A lead auditor will be nominated. The Auditee and the customer(s) will be notified of the names of the auditors and their CVs will be provided.

For auditing critical RM, SM and intermediates the number of auditors will depend on the criticality defined in agreement with the customer.

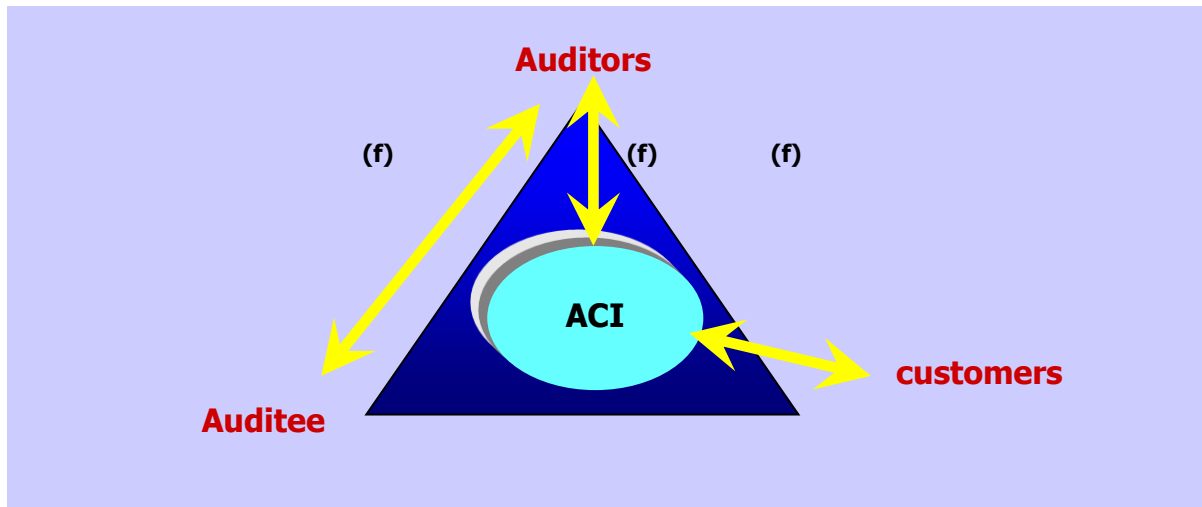
The Auditee and the customer(s) are entitled to reject the proposed auditors. Nevertheless they will be asked to explain the reasons for rejecting an auditor. In these cases new auditors will be selected by the API Compliance Institute. On request the Auditee and the customer will be informed on the types of audits the auditor(s) has/ve conducted during the past two years.

After agreement on the choice of auditors, a Secrecy Agreement (Appendix 3) will be signed by the API Compliance Institute, the customer(s), the Auditee and the Auditors. Company Secrecy Agreements may also be used.

The auditors will sign a statement in the Secrecy Agreement to confirm that they did not work for the Auditee or customer (for example as a consultant or employee) for at least 5 years prior to the audit and there is no financial interest or commercial conflict with customer or Auditee.

#### 4.1.4 Execution of the Audit

Figure 6: Steps (3) and (4): Preparing and executing the audit



(f) Lead Auditor interacts directly with the Auditee in order to plan the audit in detail. The customers will be informed by ACI.

As a guideline, the audit may be performed by two auditors for two days. The ACI will propose the duration of the Audit and number of auditors considering the scope of the audit.

If the agreed audit time schedule and/or number of auditors changes during the audit, this must be communicated immediately to the customer(s) and ACI explaining the reason for the change.

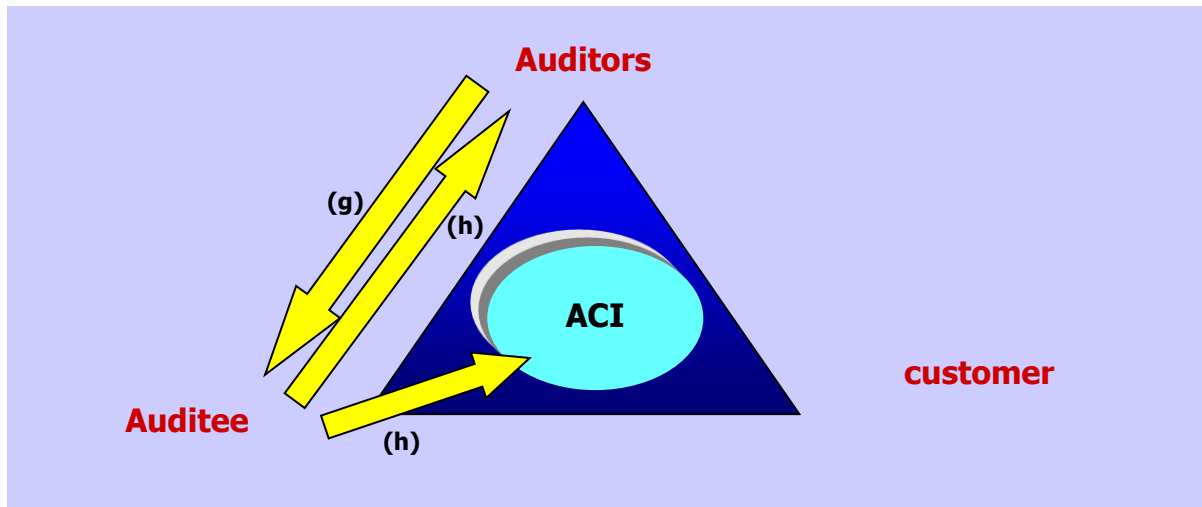
Before the audit, the Auditee will receive an audit plan from the auditors, detailing the major topics of the audit and a tentative schedule. During the audit, the cGMP compliance of the Auditee will be evaluated by the auditors on the basis of the applicable items of the ICH Q7 guideline (GMP for APIs, part II of the EU GMP Guide) and other relevant guidances if applicable (for example ISO, ICH Q9, 10, 11) using the APIC Auditing Aide Memoire and APIC How To Do ICH Q7 Guidance document as references.

All observations relating to GMP deficiencies will be stated and classified (Refer to section 1 for classification rating) during the final wrap up meeting with the Senior Management of the Auditee.

In the case where the material Manufacturer/Distributor/Broker/Importer/Packer/Re-Packer requests the Third Party Audit as part of a Self Assessment of GMP status, a 2-day audit performed by 1 auditor may be sufficient.

#### 4.1.5 Audit Report: Reviewing, Signing and Archiving

Figure 7: Step (5): Exchange of draft audit report



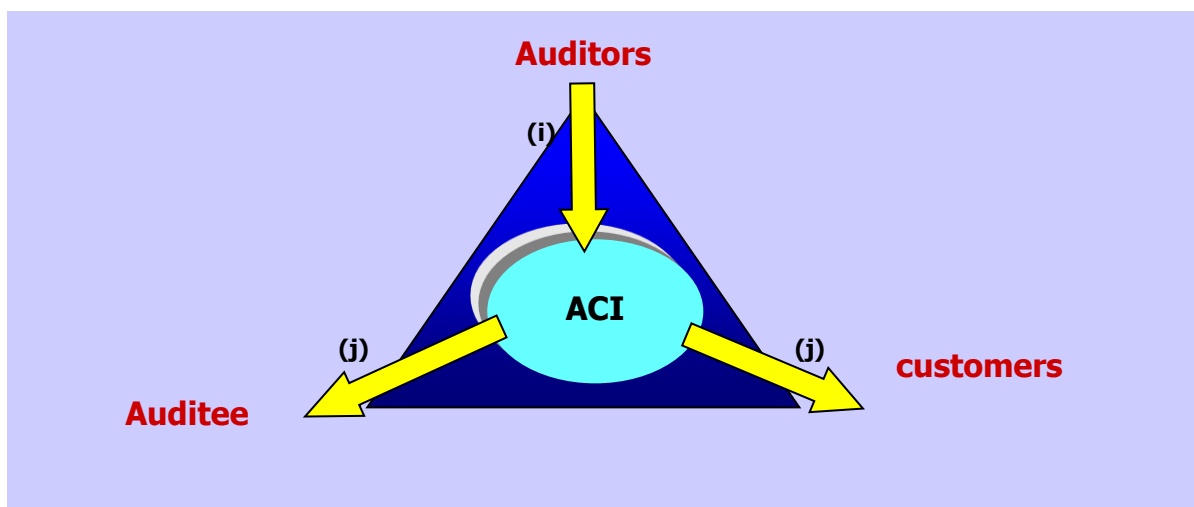
(g) Lead Auditor sends the draft audit report to the Auditee for any missing data, errors in data etc. and for defining corrective actions.

(h) After checking the draft audit report for accuracy, the Auditee responds to any observations proposing corrective actions, amends these parts to the final draft of the report and sends it back to the auditors and the ACI.

**IMPORTANT:** In the drafted report only 'factual' mistakes should be corrected.

At the latest, within a period of 3 working weeks after the audit, the lead auditor sends a drafted audit report to the Auditee to check for accuracy and to define corrective actions. The audit report will include a management summary, an overview of which ICH topics were evaluated during the Audit, supported by the ICH Q7 checklist and a detailed description and evidence of the deficiencies. The Auditee should check the accuracy and respond to any observations, proposing corrective actions, responsibilities and time frames within one month and amend these parts to the final draft of the audit report that will be sent back to the auditors and the ACI. The auditors will check within 2 weeks time whether the CAPAs are reasonable and send the signed audit report to ACI. ACI will forward the final version of the audit report to the audit initiators and the auditee.

**Figure 8: Step (6): Handover of the final audit report**



- (i) After having reviewed that proposed actions have been defined for any deficiencies the auditors sign the final audit report that is sent to the ACI.
- (j) The ACI sends copies of the signed audit report to the customer(s) and to the Auditee and archives the original signed audit report.

On receipt of the audit report from the Auditee, the auditors will review and confirm that a response with realistic timelines has been received for each observation, sign the audit report and send it to the API Compliance Institute. The ACI will then issue a copy of the final signed audit report to the customer(s) and to the Auditee.

The original audit reports are archived for 10 years, however, the original signed audit report remains valid for maximum 3 years.  
The customer(s) are responsible to review the signed audit report received and decide if any deficiencies have been adequately addressed.

The evaluation of the impact of the audit deficiencies included in the audit report on the GMP status of the API(s) used in the Manufacture of Medicinal Products is the responsibility of the Customer.

#### **4.1.6. Resolution of disagreement with GMP deficiencies/performance of auditors.**

In the case that the QP or Responsible Person of the MAH or Auditee is not satisfied with the quality of the audit report/performance of the auditors, they should contact ACI in writing explaining their concerns. ACI will review their concerns with the auditors and QP or Responsible Person of the MAH and try to satisfy the concerns. In the case that there continues to be a serious disagreement on any of the deficiencies made in the audit report or in the performance of the auditors, the ACI may also request independent review from the APIC Audit Programme Representative/APIC Excom Member on the GMP Compliance issues raised. In this case, the ACI should ensure there is no Conflict of Interest with the APIC Nominee

and the Auditee and the terms of the Confidentiality Agreement should be extended to include this review. The ACI will report in writing to the QP or Responsible Person of the MAH and the Auditee to give feedback on the formal review of their disagreements and request agreement to close the audit report.

In the case that resolution of disagreements is not possible and the disagreements are related to poor audit performance, the Audit Agreement will be revoked. Written statements of the auditors, the auditee and the customer will be included into the audit report.

**IMPORTANT:** The copyright of the audit report is jointly held by the customer(s), Auditee and API Compliance Institute. If any of these parties wishes to pass on the audit report to a subsequent Third Party, a request should be made to the API Compliance Institute.

The API Compliance Institute will discuss the use of the Third Party Audit Report with the subsequent customer to ensure the scope of the audit meets their requirements before the audit report is shared.

With the agreement of the Auditee, a list of Third Party Audits completed within the last 3 years may be published on the ACI Website.

**IMPORTANT NOTE:** It is an essential condition of the Audit Agreement that all Parties agree in advance of the audit that the audit reports may be shown to Inspectors during an audit of the customer as evidence for the qualification of the material

#### **4.2 Audit Follow-up**

Following completion and issue of the Third Party Audit Report, the Auditee should issue periodic updates on progress with proposed actions to the customer(s) based on the timelines defined in the audit report.

The customers have the responsibility to check that the proposed actions of the Auditee in response to the audit observations have been implemented in a timely and effective manner.

The customers will also decide on the need and timing for a follow up audit including auditing of the effectiveness of the corrective actions defined in original audit report.

The auditee needs to inform ACI from important changes that impact the validity of the current audit report

#### **4.3 Audit Feedback**

Within one month of completion of the audit report, the ACI will request feedback on the effectiveness of the audit process and performance of the auditors from the Auditee using the standard form (Appendix 5). Feedback on displayed knowledge and understanding of the GMP requirements for APIs, audit performance, general communication and inter-personal skills of the auditors will be requested.



This feedback will be used by ACI to improve the effectiveness of the audit programme and to assess the performance of the auditors on an ongoing basis and will be reviewed during the evaluation of auditor performance at the time of their Re-Certification as APIC Auditors.

## **5 Costs Considerations**

The costs of an audit will be calculated

- on a fee per diem rate and
- reimbursement of travelling of the Auditors.

An audit of an manufacturing site will be calculated on the following basis:

Fee 1,600.- Euro per Day and Auditor excluding travel costs.

The number of customers will be considered for the cost calculation. This can reduce the audit costs significantly.

In the case that a completed Third Party Audit Report is requested by subsequent customers, re-imburement costs will be given to the original customer(s) for the Third Party Audit until all costs of the initial audit have been reimbursed. For more details please contact the ACI.

## 6 Relationship between APIC and the API Compliance Institute

There is an Agreement between APIC and the API Compliance Institute that defines the responsibilities of each party.

Table 1 lists the major obligations of the API Compliance Institute and APIC.

Table 1: Major obligations of the API Compliance Institute and APIC

API Compliance Institute	APIC
<ul style="list-style-type: none"> <li>• Design of the Auditor qualification seminars (see 2.2)</li> <li>• Organisation and execution of the qualification seminars and examinations for Certified Auditors</li> <li>• Maintenance of Current list of APIC Certified Auditors</li> <li>• Coordination of the APIC Third Party audits</li> <li>• Steps of the audit process:               <ul style="list-style-type: none"> <li>- Preliminary Talks (see 3.1.1)</li> <li>- Preparation for the audit (see 3.1.2)</li> <li>- Selection of Auditors (see 3.1.3)</li> </ul> </li> <li>• Administration and archiving of the audit reports for 10 years</li> <li>• Compilation of an annual report for APIC</li> <li>• Re-certification review/approval</li> </ul>	<ul style="list-style-type: none"> <li>• Providing speakers for the Auditor training courses;</li> <li>• Involvement of APIC Executive and Quality Working Group members in Auditor training courses</li> <li>• APIC lead representative for audit programme to be involved in Auditor qualification courses and to evaluate suitability of candidates for APIC Certified Auditors</li> <li>• APIC lead representative for Audit programme or APIC EXEC Member to give independent review of any serious objections from the Auditee / customer to GMP Deficiencies and classifications at the request of API Compliance Institute</li> </ul>

APIC will review, on a regular basis, together with the API Compliance Institute the function of the "APIC Audit Programme" process and will agree any areas of improvements.

APIC will not intervene in the responsibilities of the API Compliance Institute related to this programme and will not request specific information related to audited companies such as audit reports.

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