Erfahrung und Umsetzung in der praktischen Tätigkeit:

Verfügbarkeit der Auditberichte API Hersteller für QP Declaration		
Auditberichte für API Intermediates*		
1. Erhalten Sie alle Auditberichte	Ja ☐	Nein ☐
- In welcher Form?		
- Vollständiger Auditbericht als Dokument (elektronisch/Papier)	Ja ☐	Nein ☐
- Durchsicht via Online Tool, aber keine physische Überlassung	Ja ☐	Nein ☐
Sonstiges:		
- Sind die Anforderungen an den Inhalt gem. Q&A Frage 8* abgedeckt?	Ja ☐	Nein ☐
2. Erhalten Sie alle CV's der durchführenden Auditoren	Ja ☐	Nein ☐
- Sind die Anforderungen an den Inhalt gem. Q&A Frage 9** abgedeckt?	Ja ☐	Nein ☐
Eigene Kommentare/ Erfahrungen:		
Auditberichte für API's		
3. Erhalten Sie alle Auditberichte	Ja ☐	Nein ☐
- In welcher Form?		
- Vollständiger Auditbericht als Dokument (elektronisch/Papier)	Ja ☐	Nein ☐
- Durchsicht via Online Tool, aber keine physische Überlassung	Ja ☐	Nein ☐
Sonstiges:		
- Sind die Anforderungen an den Inhalt gem. Q&A Frage 8* abgedeckt?	Ja ☐	Nein ☐
4. Erhalten Sie alle CV's der durchführenden Auditoren	Ja ☐	Nein ☐
- Sind die Anforderungen an den Inhalt gem. Q&A Frage 9** abgedeckt?	Ja ☐	Nein ☐
Eigene Kommentare/ Erfahrungen:		

*API Intermediates manufactured under GMP

Zur Info: Gesetzliche Vorgabe im Ramen von Inspektionen:

https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-manufacturing-practice/guidance-good-manufacturing-practice-good-distribution-practice-questions-answers#section11

*8. During inspections, why do inspectors sometimes ask to see reports of audits of active substance manufacturers carried out by the medicinal product manufacturer? H+V May 2013

As a minimum, the following is expected to be included in the report:

- The full postal address of the site. The auditors must be identified by full name and their employer recorded. If the audit is conducted on behalf of other parties this should be clear in the report. Where an audit report is obtained through a third party, the manufacturing-authorisation holder is responsible for ensuring the validity and impartiality of the audit report. The identity of key staff participating in the audit should be recorded along with their roles.The full contact details of the person through which the audit was arranged should be recorded including contact details (e-mail address, telephone number). The dates of the audit should be recorded, with the full-day equivalents clarified if full days were not spent on site. A justification should be recorded for the duration of the audit. If, in exceptional circumstances, the audit had to be restricted to fewer days on site than required by the scope of the audit, the reasons should be explained and the conclusions with respect to the GMP status of the site should be justified. Background information on the active substance manufacturer should be recorded; this should include the company ownership, the age of the site, the number of staff employed in total and for the specific products being audited. The role of the site in manufacture of the active substances being audited should also be clarified for each of the active substances being audited, e.g. if the site performs the full manufacture or only part of the manufacture.
- The scope of the audit should be clearly stated e.g. what activities (against European Union GMP part II / International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Q7 chapters) were covered. The activities which were not covered by the audit should also be clearly recorded. Auditors should identify the high risk areas for audit specific to the site or products being audited. For example, these could include but not be limited to:
    - process, cleaning or validation;
    - risk of cross-contamination with other active substances or other substances;
    - potential for generation of unknown impurities;
    - risk of mix-up of materials and products through materials handling or packing;
    - change control;
    - deviation recording or management;
    - security sealing of active substance containers and security or temperature control of shipments.
- Subsequent audits conducted as part of the ongoing supplier audit program may have a reduced scope focusing on the highest risk areas. In such cases the highest risk areas should be identified and justified.
- A list should be recorded of all active substances directly included in the audit scope plus other active substances or intermediates (or other products) manufactured at the site.

There should be a clear record of the products, the stages of manufacture and the buildings audited. If access was denied to any relevant areas of the site this should be recorded and explained. The list should clarify which of the active substances in the scope of the audit are manufactured in multi-purpose equipment or buildings as either final product or any of the intermediate stages.

- Dates of any previous audit conducted by or on behalf of the same manufacturing-authorisation holder should be recorded. If any of the audits did not conclude with a positive GMP compliance status, a brief summary of the reasons for this should be recorded.
- Each of the applicable sections of EU GMP part II should form sections of the report with a summary of what was examined, the key findings and compliance with the requirements of each section. The report should clearly state findings against each activity audited with particular focus on the high risk areas. Any GMP deficiency identified during the audit must be clearly recorded with its criticality defined. An explanation should be given, in the report or in a supporting standard operating procedure, of the categorisation system used to classify deficiencies, e.g. critical, major or minor.

- Responses to the audit by the active-substance manufacturer should be reviewed by the auditors. Corrective and preventative actions and timescales for completion should be assessed by the auditors to establish whether these are appropriate to the findings. Further clarification or evidence of completion should be requested, commensurate to the risk.
- A summary assessment of the status of corrective and preventive actions should be recorded by the auditors once these have been received and assessed. An overall recommendation should be made in the final report. The summary should include whether the auditor regards the actions as satisfactory. The responsible QP should ensure that he or she, or someone to whom it is delegated, is in agreement with the overall recommendation of the final report. The QP must not release the relevant medicinal products without knowledge of a positive recommendation from the auditors. This recommendation should include the GMP compliance status of the site and whether any reduced controls on materials receipt at the finished product manufacturing site are supported by the auditors.
- A proposed re-assessment period should be recommended.
- The final report should be signed and dated by, at least, the lead auditor.

**9. What expectations do inspectors have for the content of reports of audits of active substance manufacturers carried out by the medicinal-product manufacturer? H+V May 2013

Auditors should have sufficient scientific, technical and other experience to enable them to perform an adequate and thorough audit of the active substance manufacturer, as related to the planned scope of the audit. Where a proposed auditor lacks an appropriate level of direct experience in the field of active substance manufacture, he or she should undergo a documented training and assessment programme in the areas that are relevant to the audit, taking into account the auditor's anticipated role in the audit and the technologies that are likely to be encountered during the audit. Auditors must also be trained and assessed in their knowledge and understanding of EU GMP part II and in auditing techniques in general. The training and assessment should be fully documented.
The qualification and experience of contracted auditors are the same as the requirements for the manufacturing-authorisation holder's own auditors.