Audit Management Plan

稽核管理計畫

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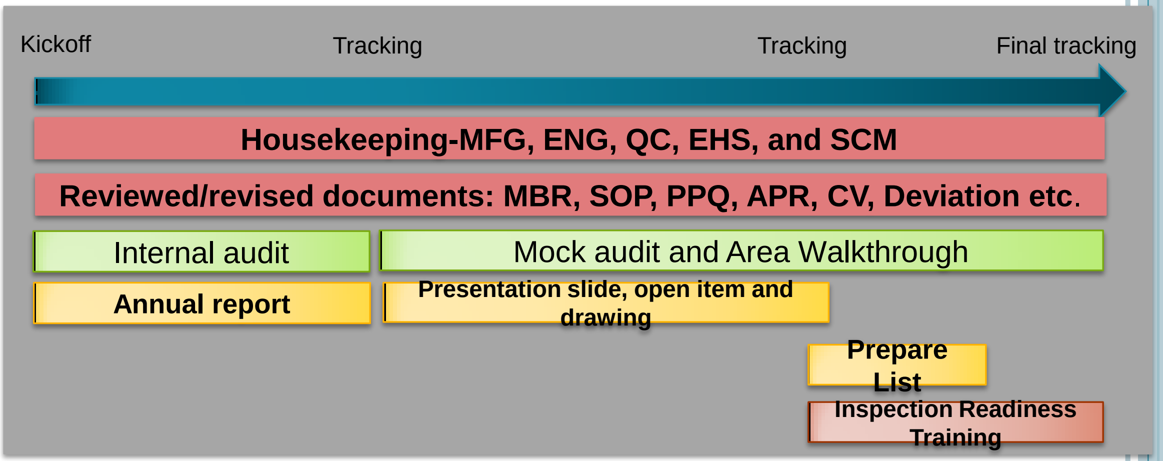
OUTLINE

- Preparation for Audit Management Team
- Preparation for SMEs
- Auditors' Expectations

PREPARATION FOR AUDIT MANAGEMENT TEAM

OVERALL READINESS



Kickoff

Tracking

Tracking

Final tracking

Housekeeping-MFG, ENG, QC, EHS, and SCM

Reviewed/revised documents: MBR, SOP, PPQ, APR, CV, Deviation etc.

Internal audit

Mock audit and Area Walkthrough

Annual report

Presentation slide, open item and drawing

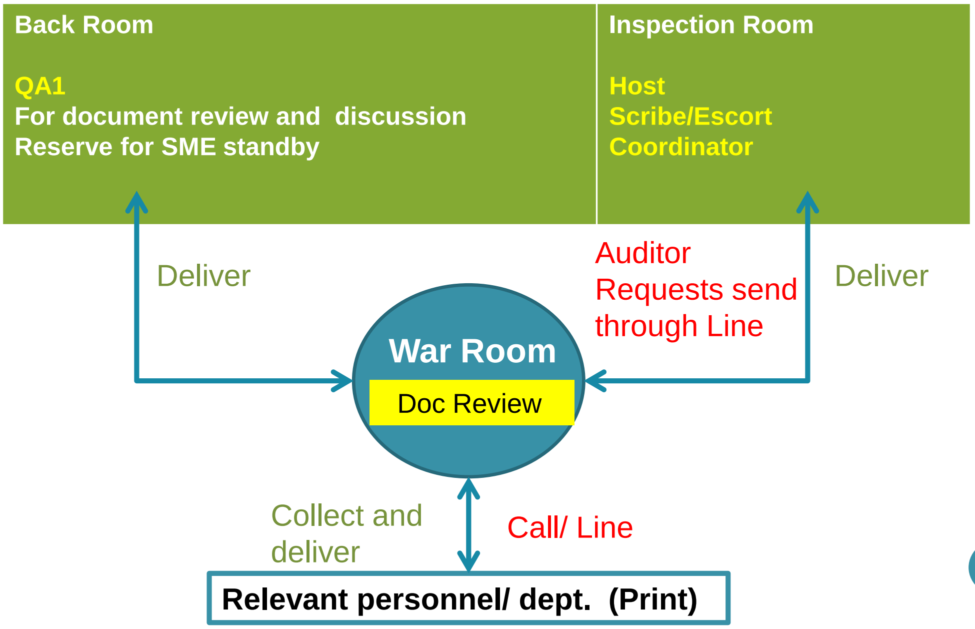
Prepare List

Inspection Readiness Training

AUDIT SCOPE

Auditor	**Background check**
Product	**All products – product list and status**
System	**Quality, Materials, Production, Facilities and Equipment, Packaging and Labeling, Laboratory and Validation**
Standard	**1. 斷層掃描用正子放射同位素優良調製作業指引** **2. 21 CFR Part 212**

INSPECTION MANAGEMENT



Back Room

QA1
For document review and discussion
Reserve for SME standby

Inspection Room

Host
Scribe/Escort
Coordinator

Deliver

Auditor Requests send through Line

Deliver

War Room

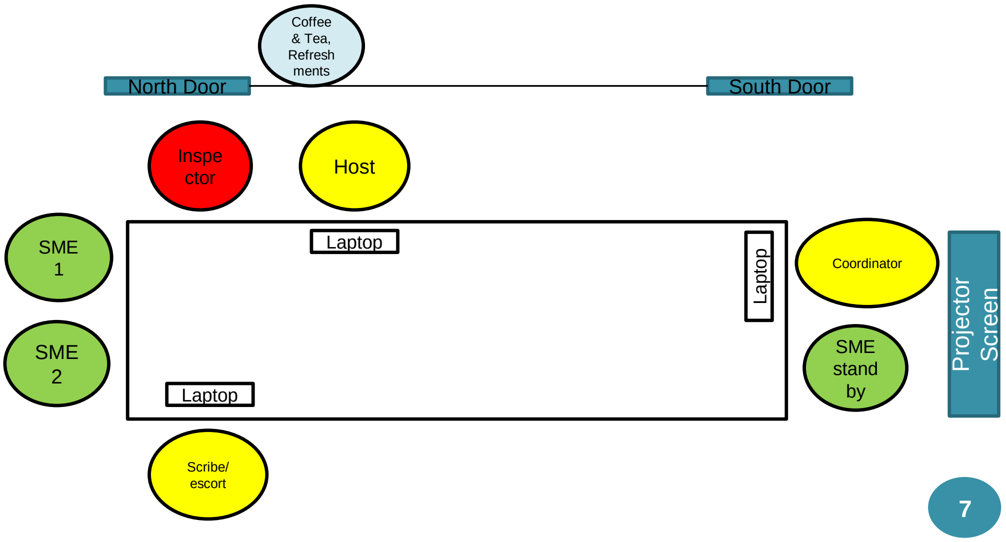
Doc Review

Collect and deliver

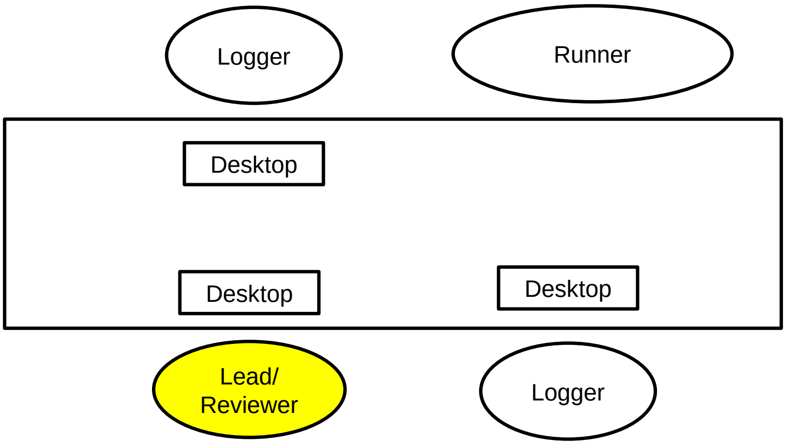
Call/ Line

Relevant personnel/ dept. (Print)

Audit Management Team-Inspection Room


Coffee & Tea, Refreshments
North Door
South Door
Inspector
Host
SME 1
SME 2
Laptop
Laptop
Laptop
Coordinator
SME stand by
Projector Screen
Scribe/ escort

War Room Management Team


Logger
Runner
Desktop
Desktop
Desktop
Lead/ Reviewer
Logger

- Connects through instant messaging
- Find documents/ answers to queries/ SMEs
- Keep logs of all items go in and out of inspection room
- Keep track every requests and time management

FLOOR PREP & TOUR GROUP

Prior to the tour, Floor manager is responsible to tour and review in the area regarding:

- Housekeeping
- Material Staging and ID Labels
- Calibration Stickers for rooms in operations

Inspection Tour Group Members:

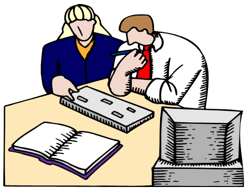
- Inspector
- Host
- Scribe/Escort
- Coordinator
- Area Department Head
- Area SMEs (limit to additional 1-2 person)

General Work Flow- Audit Management Team

- If documents are requested, **Scribe** will request them (using ** sign for ease of tracking)
- ALL requests go to the **War/Back Room via Instant messaging** (Line)
- ALL documents go to the Inspection Room **via the War/Back Room.**
- Do not hand over documents to the Inspector, unless **an reviewer have previewed**.

General Work Flow- Audit Management Team

- **Back Room** Help contact SMEs summoned to interact with the inspectors
  - No employee is considered exempt
  - We all represent the organization
- **Back Room Leader** brief to SMEs prior to entering the room
  - Why you are being questioned
  - Appropriate responses
  - Documentation preparation (if necessary)
  - Dress rehearsal



- SMEs will be accompanied by an **host/escort** at all times
  - Host/escort can intervene and help you with answers

Internal Wrap Up Meetings

- Internal Daily Wrap Up Meeting (1700-1730 daily)
  - The purpose of the daily wrap up meetings is to summarize the daily activities, potential observations and requests for the following day.
  - Individuals required to prepare information responding to inspector's requests will be identified during the daily wrap up meeting.

INSPECTION ROOM

- Inspection Rooms
- Cellular phones should not be used in the presence of inspectors and should be kept on vibrate.
- No side conversations are permitted.

BACK ROOM LEADER

- Equipped with phone (mobile), desktop, SMEs list, Tel list and document log sheet/excel sheet.
- JD:
  1. Manage activities & speed at back room/inspection room
  2. Conform auditor request
  3. Follow up for the request if not hearing back for 15 min.
  4. Contact/ brief SMEs before entering room.
  5. Quick check the completeness of documents.
  6. Send to coordinator the doc whenever is ready
  7. Update the document follow-up status
  8. Send SME to the inspection room
  9. Daily wrap up open items follow up.

DOCUMENT LOGGER & REVIEWERS

- Location: War room
- Equipped with phone (mobile), laptop, SMEs list, Tel list and document log sheet/ excel sheet.
- JD:
  1. Record auditor request
  2. Contact responsible dept. to provide/ check
  3. Ask Runner to collect and deliver
  4. Follow up for the request if not hearing back for 15 min.
  5. Check the completeness of document
  6. Record all log in/ out documents.

RUNNER

- Location: War room
- Equipped with mobile phone (Jabber account) and healthy leg
- JD:
  1. Be reachable and available at all time.
  2. Collect document request from relative dept.
  3. Deliver to doc. Logger
  4. Help follow up for document prep status.
  5. Help find SMEs. (if document logger requested)
  6. If the runners have questions about requests, they should discuss with personnel in the Back Room.

HOST

- Location: Inspection room
- Equipped with 1 laptop for quick search SOP/anything necessary.
- JD:

1. The host will serve as liaison between the inspector(s) and site personnel.
2. The host will ensure that escorts, scribes, and runners are available and coordinate daily activities.

   i.e. daily briefings, tours, and agenda topics/personnel
3. The host is responsible for communicating inspection activities to Senior Management and inspectors.
4. Translate if SMEs needed help.
5. **Stop SMEs** if they misunderstood the question.
6. **Stop SMEs** if argue in the auditing room.

Note: During translation, do not add in additional opinion/ guesses on your own.

SCRIBES/ESCORT

- Location: Inspection room
- Equipped with 1 laptop for note all request.

- JD:
  1. Accompany inspectors wherever they go.
  2. Collect request from auditor and pass to Back/War Room Leader.
  3. Request clarification on inspector's question or request.
  4. Provide doc requirement priority.
  5. Scribes will describe where/when inspectors visit each building by room number, what questions they ask, who they talk to, what documents they review, and may record any general impressions.
  6. Scribes focus on recording and try not to engage in conversation with the inspector on issues raised.

COORDINATOR

- Location: Inspection room
- Equipped with 1 laptop for information clarification.

- JD:
  1. Inform Back Room regarding auditors question. (clarification if necessary)
  2. Remind Back Room if requested documents have not deliver.
  3. Coordinate SMEs and documents in the inspection room for review.

SME List

No.	System	SME 1 (Ext #)	SME 2 (Ext #)
1	APR		

No.	System
1	APR
2	Batch Release
3	Investigations
4	CAPA
5	Change Control
6	Cleaning Validation
7	Complaints
8	Computer Systems
9	Document Control
10	Equipment Qualification
11	Equipment Maintenance
12	Facilities
13	Internal Audits
14	Laboratory (Including Method validation/verification)
15	Management Review

No.	System
16	Materials Management and Distribution
17	Material Qualification
18	Packaging and Labeling
19	Preventive Maintenance / Calibration
20	Process Validation
21	Product Return and Salvage
22	Production
23	Quality Systems
24	Recall
25	Reprocess/Rework
26	Retention Samples
27	Stability
28	Training
29	Supplier Management
30	Environmental Monitoring

Final Notes

1. **Never** leave an auditor alone in the inspection room.
2. Provide a **quiet environment** in the inspection rooms whereby the auditor is able to focus on his tasks; do not have employees waiting, talking, laughing, etc. outside the inspection room.
3. **Do not provide** the auditor with **original documents** because of the risk that they get lost or misplaced.
4. Make sure you deliver the documents which have been requested by the auditor; **do not let him have to repeat his request**.
5. Make sure to have **brief introduction presentations** available to introduce complex topics or issues with the auditor.
6. For **utility systems and material, personnel and waste flows** ensure that the drawings are available in **A3 size** and be able to talk them through in detail.
7. **Clean all areas** even if not GMP areas - just in case the inspector wants to check
8. **All deviations associated with validations should be reviewed** in advance and **rehearsals** to explain logically what happened should be carried out.

PREPARATION FOR SMEs

OVERVIEW

- In this session, you will learn how to prepare yourself for an upcoming inspection:
  - Activities to perform prior to a scheduled inspection
  - Common inspector techniques
  - Dos and Don’ts when interacting with an inspector
- You will also learn the basics of the Inspection Readiness Plan and inspection logistics

How can we get prepared so that it will lead to a successful inspection?

The Inspection & Inspectors

- Nothing replaces good judgment and preparedness
  - We must have a plan…inspectors have one
    - - Investigations Operations Manual (IOM)
    - - The Quality System Inspection Technique (QSIT)
    - - *Inspection Guides*

  - We must know what to do from initial contact through end of inspection
  - We must strategize / prepare / conduct mock inspection
  - We must take immediate actions / assemble team / staff War Room

The Inspection & Inspectors

- There are no ***“Absolutes”***
- Inspectors looking for compliance to cGMP
- All inspectors are different
  - Background
  - Experience
  - Bias
- All situations are different
  - Pre-approval (PAI)
  - Routine
  - For cause

The Inspection & Inspectors

WHAT ARE THE BASIC AREAS OF INTEREST TO MOST INSPECTORS?

- Do you know…
  - -WHAT you are doing?
  - -WHY you are doing it?

- Do you have an evidence to show you have done it correctly?

- Is everything (systems) under control?

The Inspection & Inspectors

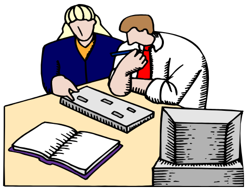
- If documents are requested, your escort will request them

  -Escorts / Scribes / SMEs should anticipate inspection paths
- *ALL* requests go to the War Room via Instant messaging
- *ALL* documents go to the Inspection Room via the War Room
- Do not hand over documents to the inspector, until you *and* an escort or reviewer have previewed them

  -Only obtain documents from their official source location

Handling Inspector Questions

- You may be summoned to interact with the inspector
    - No employee is considered exempt
    - We all represent the organization
- You will be briefed prior to entering the room
    - Why you are being questioned
    - Appropriate responses
    - Dress rehearsal
- You will be accompanied by an escort at all times
    - Escort is at your side
    - They can intervene and help you with answers



Handling Inspector Questions

- Introduction to investigators
    - Business card / shake hands if appropriate
    - Cordial / professional
- The inspectors assume they are interviewing someone who has been trained to interact with them
    - As compliance concerns increase, so does the depth of investigation
    - Personnel interviews
- Listen carefully to questions and make sure you understand them
- Repeat back the question to investigator ask for clarification if needed
- Respond directly to questions and answer truthfully

Handling Inspector Questions

- Answer questions with confidence, speaking slowly and clearly
- Keep Responses short
- Avoid defensive postures
- Keep a professional demeanor
- Be attentive and give positive feedback to show that you are listening

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PHRASES TO AVOID

- " I think……"
- "Sometimes…."
- "Not my responsibility…."
- "It's too expensive…."
- "Usually…."

PHRASES TO AVOID

- “ That should not have happened….”
- “To be honest….”
- “Probably…..”
- “It should be….”
- “Not enough staff”
- “It was before my time”

Handling Inspector Questions

- Remember that an appropriate answer is:
- ***“I’m not sure, I’ll find out and get back to you.”***
- Note commitments and be sure to follow up as soon as possible on things that you have committed to do
- If you feel a need to bring someone into the room to answer a question, do not bring them in without consulting the escort

Basic Inspection Behaviors

DO NOT……

- Act nervous
- Mislead the investigator
- Lie to the investigator
- Interfere with the escort/inspection team
- Argue with the investigator
- Sign any document unless advised by the escort
- Take inspector to any area without an escort

Basic Inspection Behaviors

DO……

- Provide prompt and courteous responses and retrieval
  - Slow responses may raise suspicion that something is wrong or out of control
  - The investigator will follow up to ensure receipt of information
- Respond through the inspection team whenever possible
  - Provide short succinct answers via war room to Inspection Room
  - Minimize visits to the Inspection Room if possible
- Attempt to limit the scope of the questions by referencing a time period (e.g. the last month)

Basic Inspection Behaviors

DO……

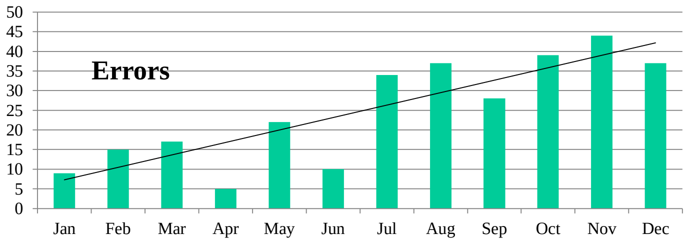
- Anticipate inspectors visit to your work area:
  - Make sure area is neat, tidy, organized
  - Remove any physical items that could prompt questions

    -Remove product materials from non-production areas

Basic Inspection Behaviors

DO……

- Remove questionable wall postings, charts, graphs, memos, overdue training notices, etc…



Basic Inspection Behaviors

DO……

- Use the SOPs to aid in answering questions for complex operations or processes
- Use the SOPs only if you are familiar with their content
- Reference only the section(s) of the SOP to address the question

Basic Inspection Behaviors

DO NOT……

- Answer questions that are not 100% clear to you
- Guess
- React emotionally
- Provide your opinions
- Answer for someone else
- Answer questions that do not pertain to your department or operations

Responding To Inspector Questions Is Not The Time To Show How Much You *Know*…or *Don't Know*

Basic Inspection Behaviors

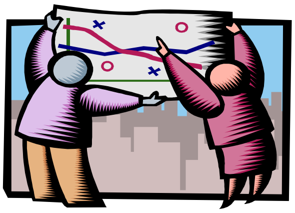
DO NOT……

- Interpret, or “read into” the investigator’s questions

  -“Do you mean that …”

  -“Do you really want to see …”

  -“I know what you’re getting at…”



Inspector Interview Techniques

- Deliberate Pause
- Ask same question different ways
- Ask open ended questions
  - Inspector: “Please tell me how you handle changes at your site.”
  - Your Response: “What specifically would you like to know?”
  - Inspector: “What is your SOP for handling changes for commercially distributed product?”

Inspector Interview Techniques

DO NOT……

Include an ***invitation*** to your response

… ***"would you like to see…"***

… "could I get a copy…"

… "would you like to speak to … or review…"

Any information you volunteer to inspector can remind them to inspect something else.

Inspector Interview Techniques

DO NOT……

- Answer "off the record" questions
- Do not volunteer demonstrations without discussion and planning with your management and the inspection team
- Answer opinion type questions
  - ***"What do you think"***
  - ***"What is you best guess"***
  - ***"What would you do …"***
- Do not speculate

Inspector Interview Techniques

DO NOT……

- Provide approximate numbers, occurrences and percentages

  "How many failures …"

  "How many times …"

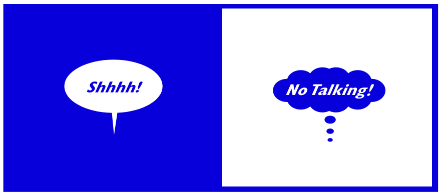
  "Give me a ballpark figure …"

Inspector Interview Techniques

DO NOT……

- Engage in side discussions or "filler" dialogue.

"When the investigator stops speaking, it does not mean it is time for you to start speaking"


Shhhh!
No Talking!

Inspector Interview Techniques

DO……

- ➢ Insist on answering after reviewing the appropriate records
- ➢ If you respond to a question incorrectly, and later find out that you were wrong, correct yourself for the record

Inspector Interview Techniques

DO NOT……

- ➢ Point out errors
- ➢ Comment or "apologize" for the quality of the data
- ➢ Comment on plans to improve record keeping practices, unless criticized by the investigator
- ➢ Correct errors during the review
- ➢ Make constant references to planned SOP revisions, unless criticized by the investigator

Inspector Interview Techniques

DO NOT……

- Use the inspector as your consultant
- Do not leave the inspector alone unless they request to be alone
- Do not change a document that inspector has seen and requested a copy of before you copy it

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Final Tips

- Let your management know where you are at all times
- Make sure your management & escort see documents that you are giving to the inspector
- Don’t use cell phone in the conference room
- Don’t discuss the content of documents with messengers who deliver them to the room
- If you leave the room to talk, be out of earshot

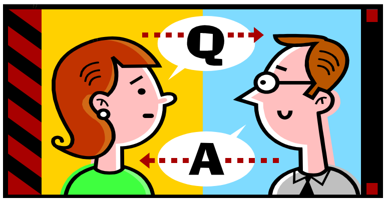
Final Tips

- Include only the information requested by the investigator when supplying additional documentation
- Don’t bring anything into the room
- Inspection team should capture the same photograph if taken by inspector (what is our policy?)

Final Tips

- Be conscious of your conversations in public settings
- Inspectors can observe and question anything in their view

Remember: You are a GMP professional. Even though the inspector controls the question, you control your response



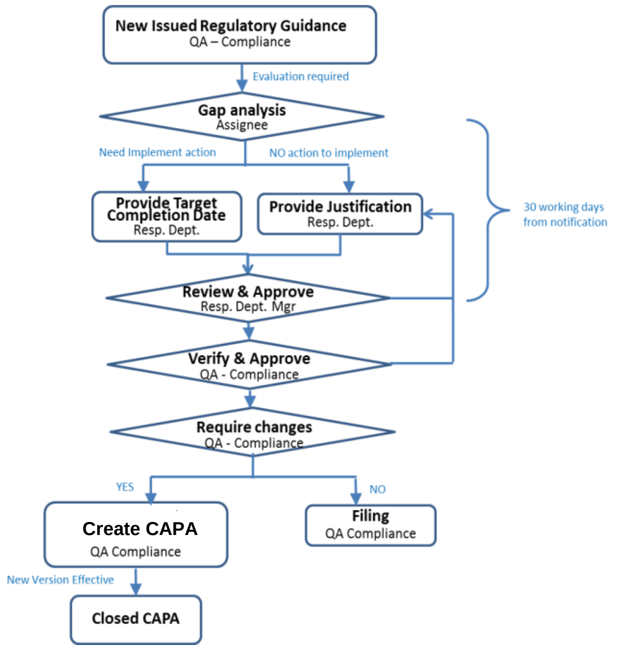
Final Tips

- Be truthful
- Be prompt
- Be cooperative
- Do not volunteer information
- Answer exactly what you are asked
- Keep your management aware

SUMMARY

- **Everyone is important during an inspection**
- **Inspection Readiness is a state in which we live, not react to**
- **You do your job right every day, during an inspection is no different**

Regulatory Gap Assessment


New Issued Regulatory Guidance
QA – Compliance
Evaluation required
Gap analysis
Assignee
Need Implement action
NO action to implement
Provide Target Completion Date
Resp. Dept.
Provide Justification
Resp. Dept.
30 working days from notification
Review & Approve
Resp. Dept. Mgr
Verify & Approve
QA - Compliance
Require changes
QA - Compliance
YES
NO
Create CAPA
QA Compliance
Filing
QA Compliance
New Version Effective
Closed CAPA

Regulatory Gap Assessment

表單編號: ____________________

法規名:

法規版次 : ______________________ □ N/A

段落	法規需求	SOP 號碼 & 章節號碼	缺失描述/無缺失解釋

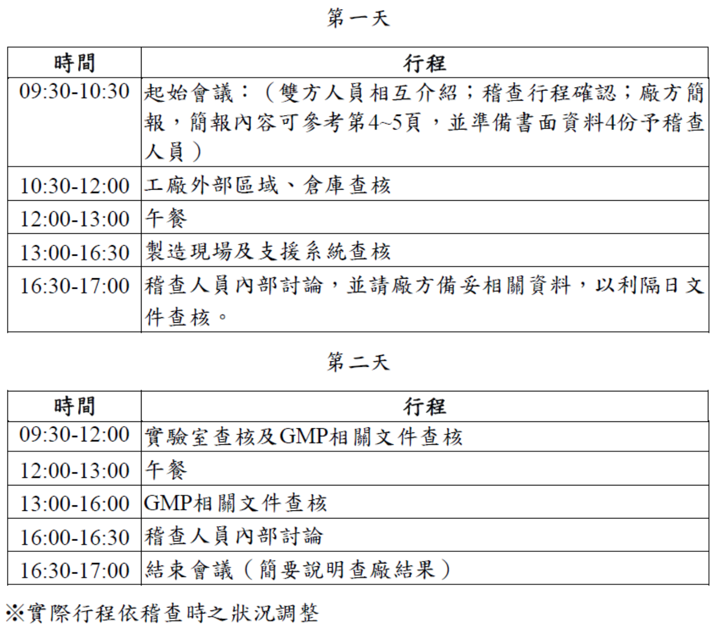
SOP 改版需求? Yes ___ No ___

預計改版日期 ____________________

執行者/日期: ____________________________ 簽合者/日期: ________________________________

AUDITOR’S EXPECTATIONS

Proposed Agenda



第一天

時間	行程
09:30-10:30	起始會議：（雙方人員相互介紹；稽查行程確認；廠方簡報，簡報內容可參考第4~5頁，並準備書面資料4份予稽查人員）
10:30-12:00	工廠外部區域、倉庫查核
12:00-13:00	午餐
13:00-16:30	製造現場及支援系統查核
16:30-17:00	稽查人員內部討論，並請廠方備妥相關資料，以利隔日文件查核。

第二天

時間	行程
09:30-12:00	實驗室查核及GMP相關文件查核
12:00-13:00	午餐
13:00-16:00	GMP相關文件查核
16:00-16:30	稽查人員內部討論
16:30-17:00	結束會議（簡要說明查廠結果）

※實際行程依稽查時之狀況調整

Pre-request Documents

查廠當天請準備

1. 查廠簡報(含紙本)
2. 清晰可視之廠房、水系統及空調系統平面圖(A3)
3. 查廠期間之生產排程

請貴廠準備下列資料，供查廠人員攜回

1. 簡報資料含電子檔
2. GMP 藥廠現況調查表(若有更新)
3. 最新中文工廠基本資料含電子檔 (若有更新)
4. GMP 藥品清冊 (若有更新)

Pre-request Documents

請提供簡報書面資料或電子檔予查廠人員，內容格式如下：

※因時間有限，請將簡報重點放在有畫線項目；其他部分由稽查員視須要提問或自行閱讀

1.藥廠整體概況

一、 藥廠簡介。

二、 生產範圍(西藥？中藥？原料藥？ 動物用藥？食品？化妝品？醫療器材？藥品輸入？)，有兼製請敘述於何處生產，及廠房、設施、設備共用情形。

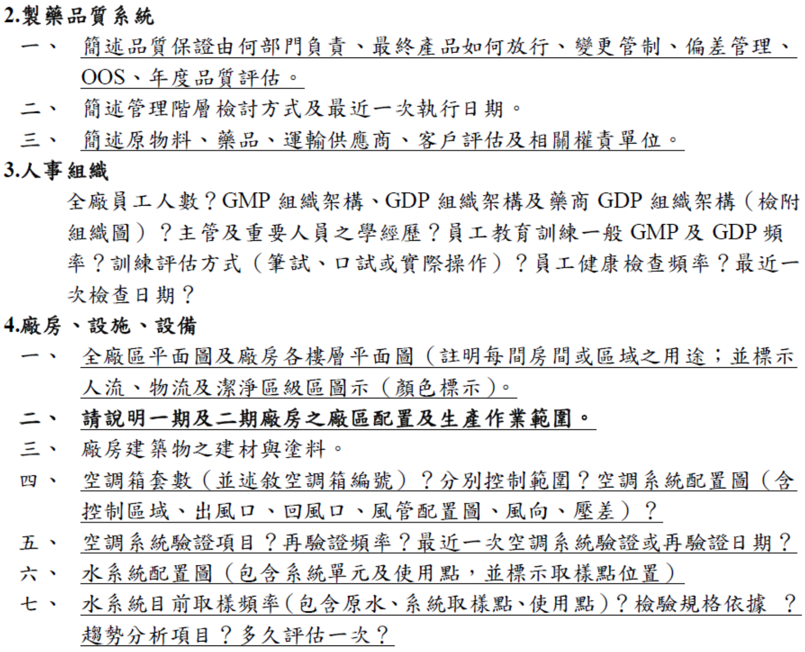
三、 特殊產品：是否生產青黴素？頭孢子菌素？Carbapenem？女性荷爾蒙？男性荷爾蒙？一般抗生素？生物藥品？抗癌藥？若有生產請敘述於何處生產，及廠房、設施、設備共用情形，另請詳述防止交叉汙染措施。

四、 儲存產品(西藥？中藥？原料藥？ 動物用藥？食品？化妝品？醫療器材？藥品輸入？管制藥品?特殊產品?)，請敘述於何處儲存，是否共用儲位情形。

五、 說明廠內生產劑型（煩請依 107 年 6 月 11 日衛授食字第 1071103236 號函之「西藥製造許可及 GMP 核定項目與作業內容之藥品劑型分類原則」敘述，屆時與核備函通過劑型有關，請正確敘述；若為無菌製劑，請說明該劑型為「最終滅菌」或「無菌製備」） 。

六、 廠內生產西藥製劑許可證張數？廠內持有許可證張數？委託製造許可證張數？分別完成確效張數？

Pre-request Documents



2.製藥品質系統

一、 簡述品質保證由何部門負責、最終產品如何放行、變更管制、偏差管理、OOS、年度品質評估。

二、 簡述管理階層檢討方式及最近一次執行日期。

三、 簡述原物料、藥品、運輸供應商、客戶評估及相關權責單位。

3.人事組織

全廠員工人數？GMP 組織架構、GDP 組織架構及藥商 GDP 組織架構（檢附組織圖）？主管及重要人員之學經歷？員工教育訓練一般 GMP 及 GDP 頻率？訓練評估方式（筆試、口試或實際操作）？員工健康檢查頻率？最近一次檢查日期？

4.廠房、設施、設備

一、 全廠區平面圖及廠房各樓層平面圖（註明每間房間或區域之用途；並標示人流、物流及潔淨區級區圖示（顏色標示）。

二、 請說明一期及二期廠房之廠區配置及生產作業範圍。

三、 廠房建築物之建材與塗料。

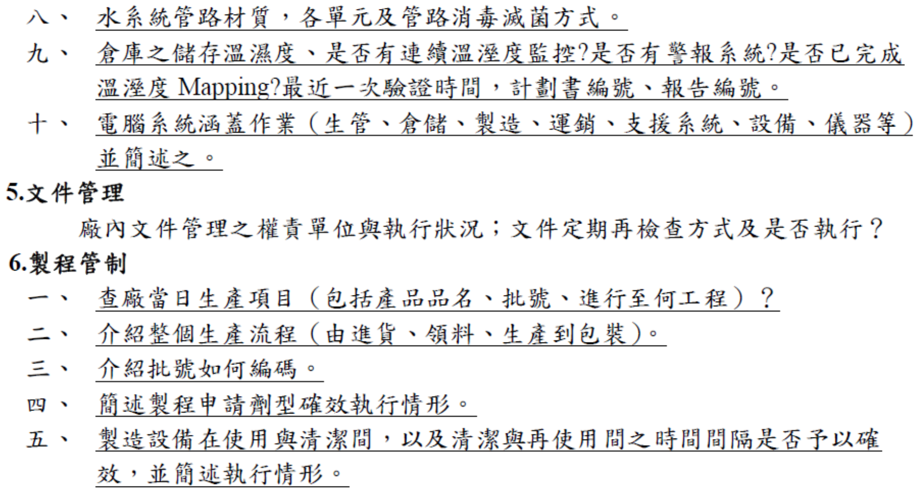
四、 空調箱套數（並述敘空調箱編號）？分別控制範圍？空調系統配置圖（含控制區域、出風口、回風口、風管配置圖、風向、壓差）？

五、 空調系統驗證項目？再驗證頻率？最近一次空調系統驗證或再驗證日期？

六、 水系統配置圖（包含系統單元及使用點，並標示取樣點位置）

七、 水系統目前取樣頻率(包含原水、系統取樣點、使用點)？檢驗規格依據 ？趨勢分析項目？多久評估一次？

Pre-request Documents



八、 水系統管路材質，各單元及管路消毒滅菌方式。

九、 倉庫之儲存溫濕度、是否有連續溫溼度監控?是否有警報系統?是否已完成溫溼度 Mapping?最近一次驗證時間，計劃書編號、報告編號。

十、 電腦系統涵蓋作業（生管、倉儲、製造、運銷、支援系統、設備、儀器等）並簡述之。

5.文件管理

廠內文件管理之權責單位與執行狀況；文件定期再檢查方式及是否執行？

6.製程管制

一、 查廠當日生產項目（包括產品品名、批號、進行至何工程）？

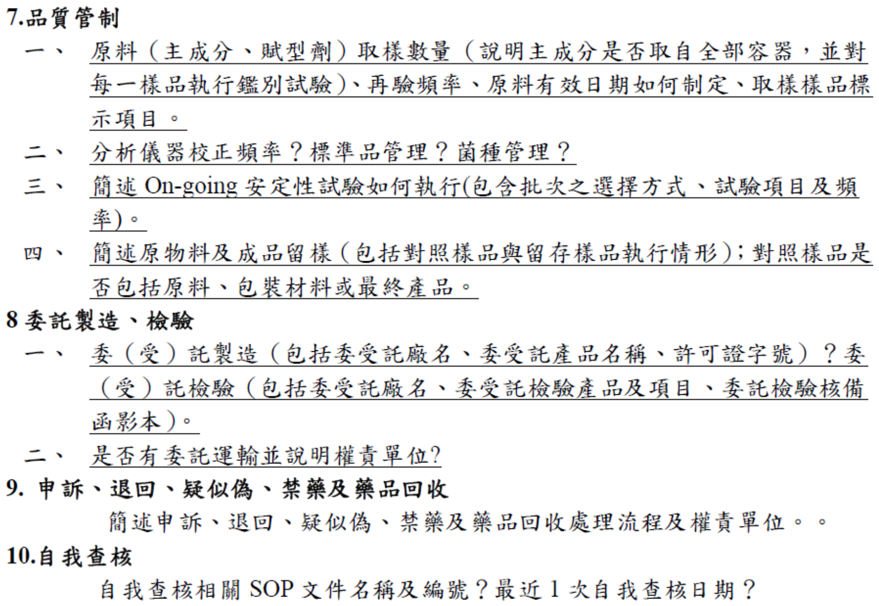
二、 介紹整個生產流程（由進貨、領料、生產到包裝）。

三、 介紹批號如何編碼。

四、 簡述製程申請劑型確效執行情形。

五、 製造設備在使用與清潔間，以及清潔與再使用間之時間間隔是否予以確效，並簡述執行情形。

Pre-request Documents



7.品質管制

一、 原料（主成分、賦型劑）取樣數量（說明主成分是否取自全部容器，並對每一樣品執行鑑別試驗）、再驗頻率、原料有效日期如何制定、取樣樣品標示項目 。

二、 分析儀器校正頻率？標準品管理？菌種管理？

三、 簡述 On-going 安定性試驗如何執行(包含批次之選擇方式、試驗項目及頻率)。

四、 簡述原物料及成品留樣（包括對照樣品與留存樣品執行情形）；對照樣品是否包括原料、包裝材料或最終產品。

8 委託製造、檢驗

一、 委（受）託製造（包括委受託廠名、委受託產品名稱、許可證字號）？委（受）託檢驗（包括委受託廠名、委受託檢驗產品及項目 、委託檢驗核備函影本)。

二、 是否有委託運輸並說明權責單位?

9. 申訴、退回、疑似偽、禁藥及藥品回收

簡述申訴、退回、疑似偽、禁藥及藥品回收處理流程及權責單位。。

10.自我查核

自我查核相關 SOP 文件名稱及編號？最近 1 次自我查核日期？

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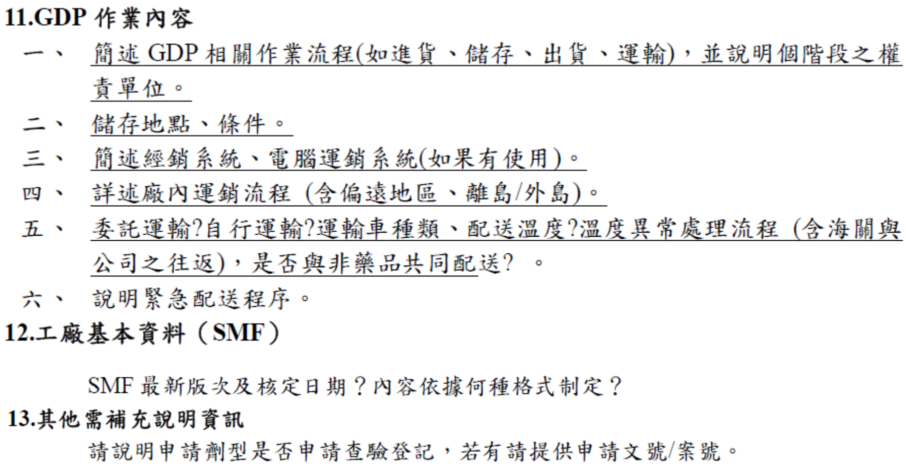
Pre-request Documents



11.GDP 作業內容

一、 簡述 GDP 相關作業流程(如進貨、儲存、出貨、運輸)，並說明個階段之權責單位。

二、 儲存地點、條件。

三、 簡述經銷系統、電腦運銷系統(如果有使用)。

四、 詳述廠內運銷流程 (含偏遠地區、離島/外島)。

五、 委託運輸?自行運輸?運輸車種類、配送溫度?溫度異常處理流程 (含海關與公司之往返)，是否與非藥品共同配送? 。

六、 說明緊急配送程序。

12.工廠基本資料（SMF）

SMF 最新版次及核定日期？內容依據何種格式制定？

13.其他需補充說明資訊

請說明申請劑型是否申請查驗登記，若有請提供申請文號/案號。

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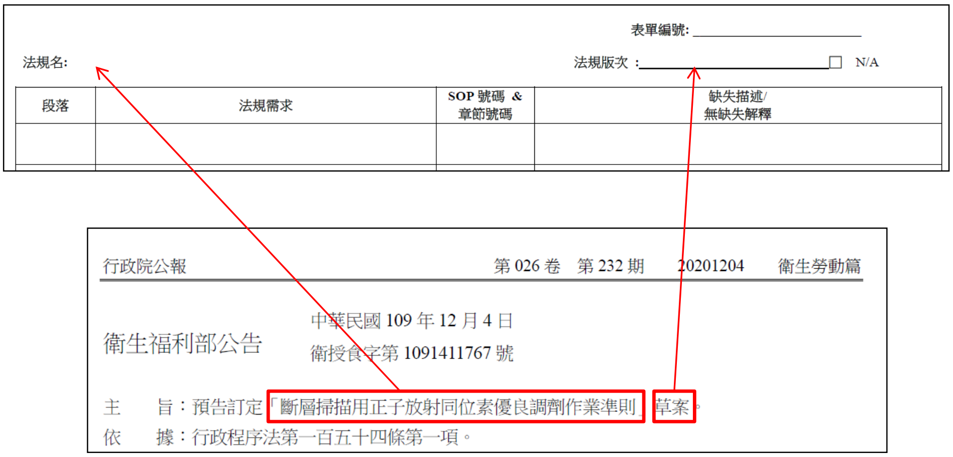
Questions?

Regulatory Gap Assessment – Workshop



表單編號: ____________________

法規名:

法規版次 : ____________________ □ N/A

段落	法規需求	SOP 號碼 & 章節號碼	缺失描述/ 無缺失解釋

行政院公報 第 026 卷 第 232 期 20201204 衛生勞動篇

衛生福利部公告

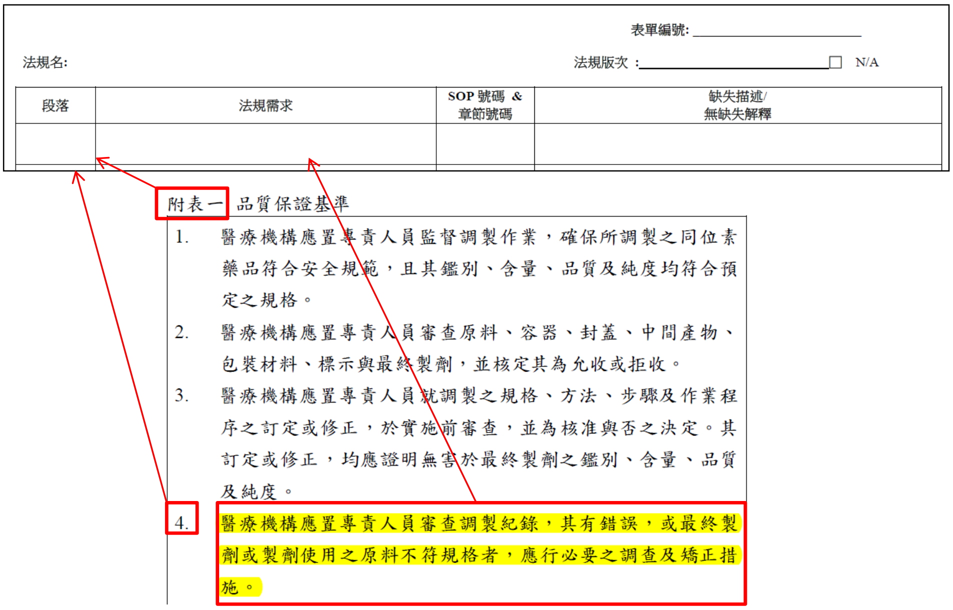
中華民國 109 年 12 月 4 日

衛授食字第 1091411767 號

主 旨：預告訂定「斷層掃描用正子放射同位素優良調劑作業準則」草案。

依 據：行政程序法第一百五十四條第一項。

Regulatory Gap Assessment – Workshop



表單編號: ____________________

法規名:

法規版次 :____________________ □ N/A

段落	法規需求	SOP 號碼 & 章節號碼	缺失描述/ 無缺失解釋

附表一 品質保證基準

1. 醫療機構應置專責人員監督調製作業，確保所調製之同位素藥品符合安全規範，且其鑑別、含量、品質及純度均符合預定之規格。
2. 醫療機構應置專責人員審查原料、容器、封蓋、中間產物、包裝材料、標示與最終製劑，並核定其為允收或拒收。
3. 醫療機構應置專責人員就調製之規格、方法、步驟及作業程序之訂定或修正，於實施前審查，並為核准與否之決定。其訂定或修正，均應證明無害於最終製劑之鑑別、含量、品質及純度。
4. 醫療機構應置專責人員審查調製紀錄，其有錯誤，或最終製劑或製劑使用之原料不符規格者，應行必要之調查及矯正措施。