COMBINATION PRODUCTS
DEVICE SPECIALISTS®

GAP analysis and audit for Combination Products

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Global regulatory harmonization for combination products with the planned QMSR regulation, asks for a new GAP analysis approach.

This approach extends the CPDS methodology, which has been utilized for many years. It involves assessing each external regulatory requirement to determine its coverage within the cGMP quality system. The new global approach for combination products is designed to enhance this process.

– For Europe (EU):

- EU medicinal product Directive 2001/83/EC and the related Pharmaceuticals Quality System requirements, as set forth in Eudralex Vol. 4 Ch. I
- European Medical Device Regulations MDR 2017/745
- EMA Guideline on quality requirements for medicinal products used with medical devices (EMA/CHMP/QWP/BWP/259165/2019), EMA Questions & Answers (Rev 2 – June 2021) on Implementation of the Medical Devices and In Vitro Diagnostic Medical Devices Regulations ((EU) 2017/745 and (EU) 2017/746)).

– For US:

- 21 CFR PART 3.2 Product Jurisdiction – Definition,
- 21 CFR PART 4 Regulation of Combinations product,
- 21 CFR PART 862-892 Devices Regulations,
- 21 CFR PART 820 Quality System Regulation. (With the mandatory revision of 21 CFR 820 effective February 2, 2026 (transitioning QSR to QMSR based on ISO 13485:2016),

– For both EU and US:

ICH Guidelines Q8 – Pharmaceutical development, Q9 – Quality risk management and Q10 – Pharmaceutical quality system.

Goal: Manufacturers can (after the required updates) demonstrate compliance with each applicable CGMP requirement for constituent parts and combination products.

All regulatory requirements should be traceable to specific processes and components within the QMS.

Gap analysis is a joint effort between CPDS expert and the company Quality system specialists. This guarantees a smooth requirements and rapid assessment of all regulatory requirement, indicating how and where they are intended to be fulfilled.

Overall Process of our GAP analysis (and further)

- Determine scope and objective
- Gather and train team members
- Identify compliance and gaps
- Present results
- -> End of GAP analysis
- Prioritize gaps with Leadership team
- Develop solutions
- Make an action plan
- Execute the plan
- Start audit sequence

We have learned to use a simple expression for the status of a requirement/situation:

1. Green: Good to go, ready

2. Orange: Depending on circumstances this requirement can result in a "finding" or Non-Conformity. Improve ASAP.

3. Red: Has to change ASAP.

Like a traffic light. Benefit: Everybody understands it, without discussion.

Important and often violated:

Implementation process audits can only be performed of cGMP systems that are overall in compliance with the regulations. In audit technical terms, implementation process audits can only be performed once the audit of the documented quality system is completed.

Be the best & save money

CPDS has developed a coherent series of trainings and services for the Pharma combination product manufacturers and their suppliers. The methods used are proven and mature (30 years experience). When followed and applied, Quality Management will become:

- Robust
- Efficient
- Mature
- Globally harmonized

Read more in the recent published white paper (+ link)

Target organizations

This GAP analysis is tailored for pharmaceutical organizations and their suppliers who are in the process of integrating all cGMP requirements, including QMSR, for combination products. Pur program is especially beneficial for midsize and small organizations.

Custom

Our GAP analysis is tailored to each individual client, with varying scopes and priorities based on their specific needs. CPDS offers the necessary regulatory building blocks to support this process. Contact us to explore the possibilities.

Availability and Costs:

The GAP analysis is an onsite process (reporting is done off-site). The costs are calculated per man-day spend. Contact us for available time window.

Duration:

With sufficient support (2-3 company Quality system experts) most results will be available within one week. Preliminary results will be presented on the last on-site day. Report will follow ASAP.

Requirement:

The pharmaceutical organization should have a process interaction map available. CPDS can provide support if needed.

Compliance map:

Even this EU site we could bring with a team into compliance (all green).

Reds and oranges became all green!

EU GMP compliance overview matrix

Question no:	Pharmaceutical Quality System	Primary Processes,	Personnel	Premise and Equipment	Documentation	Production	Quality Control	Outsourced activities	Complaints and product recalls	Self-Inspection	Site Master File	Change Control (part of Annex 15)	Risk Management Q9	Annex I Manufacturing of Sterile Medicinal products	Annex 16 Certification by a QP and Batch release	Annex 8 Sampling of starting and packaging materials	Annex 11: Computerized system	Annex 15: Qualification /Validation
01	PQS_01	PP_A_01	PER_01	P&E3_01	DOC_01	PROD_01	QC_01	OA_01	C&P_01	SI_01	SMF_01	CC_01	RM_01	STER_01	QP_01	SSP_01	COM_01	VAL_1.1
02	PQS_02	PP_A_02	PER_02	P&E3_02	DOC_02	PROD_02	QC_02	OA_02	C&P_02	SI_02	SMF_02	CC_02	RM_02	STER_02	QP_02	SSP_02	COM_02	VAL_1.2
03	PQS_03	PP_A_03	PER_03	P&E3_03	DOC_03	PROD_03	QC_03	OA_03	C&P_03	SI_03	SMF_03	CC_03	RM_03	STER_03	QP_03	SSP_03	COM_03	VAL_1.3
04	PQS_04	PP_A_04	PER_04	P&E3_04	DOC_04	PROD_04	QC_04	OA_04	C&P_04		SMF_04	CC_04	RM_04	STER_04	QP_04	SSP_04	COM_04	VAL_1.4
05	PQS_05	PP_A_05	PER_05	P&E3_05	DOC_05	PROD_05	QC_05	OA_05	C&P_05		SMF_05	CC_05	RM_05	STER_05	QP_05	SSP_05	COM_05	VAL_1.5
06	PQS_06		PER_06	P&E3_06	DOC_06	PROD_06 NA	QC_06	OA_06	C&P_06		SMF_06	CC_06	RM_06	STER_06	QP_06		COM_06	VAL_1.6 N/A
07	PQS_07		PER_07	P&E3_07	DOC_07	PROD_07	QC_07	OA_07	C&P_07		SMF_07	CC_07		STER_07	QP_07		COM_07	VAL_1.7 N/A
08	PQS_08		PER_08	P&E3_08	DOC_08	PROD_08	QC_08	OA_08	C&P_08		SMF_08			STER_08	QP_08		COM_08	VAL_1.8
09	PQS_09		PER_09	P&E3_09	DOC_09	PROD_09	QC_09	OA_09	C&P_09		SMF_09			STER_09	QP_09 NA		COM_09	VAL_2.1
10	PQS_10		PER_10	P&E3_10	DOC_10	PROD_10	QC_10	OA_10	C&P_10		SMF_10			STER_10	QP_10		COM_10	VAL_2.2
11	PQS_11		PER_11	P&E3_11	DOC_11	PROD_11	QC_11	OA_11	C&P_11					STER_11	QP_11 NA		COM_11	VAL_2.3
12	PQS_12	PP_B_01	PER_12	P&E3_12	DOC_12	PROD_12	QC_12	OA_12	C&P_12					STER_12	QP_12		COM_12	VAL_2.4
13	PQS_13	PP_B_02	PER_13	P&E3_13	DOC_13	PROD_13	QC_13	OA_13	C&P_13					STER_13	QP_13		COM_13	VAL_2.5
14		PP_B_03	PER_14	P&E3_14	DOC_14	PROD_14	QC_14	OA_14	C&P_14					STER_14			COM_14	VAL_2.6
15			PER_15	P&E3_15	DOC_15	PROD_15	QC_15	OA_15	C&P_15					STER_15			COM_15	VAL_2.7
16			PER_16	P&E3_16	DOC_16	PROD_16	QC_16	OA_16	C&P_16					STER_16			COM_16	VAL_2.8
17			PER_17	P&E3_17	DOC_17	PROD_17	QC_17	OA_17	C&P_17					STER_17			COM_17	VAL_2.9
18			PER_18	P&E3_18	DOC_18	PROD_18	QC_18		C&P_18					STER_18				VAL_2.10
19			PER_19	P&E3_19	DOC_19	PROD_19	QC_19		C&P_19					STER_19				VAL_3.1
20			PER_20	P&E3_20	DOC_20	PROD_20	QC_20		C&P_20					STER_20				VAL_3.2
21			PER_21	P&E3_21	DOC_21	PROD_21	QC_21		C&P_21					STER_21 NA				VAL_3.3
22			PER_22	P&E3_22	DOC_22	PROD_22	QC_22		C&P_22					STER_22 NA				VAL_3.4
23			PER_23	P&E3_23	DOC_23	PROD_23	QC_23		C&P_23					STER_23 NA				VAL_3.5

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