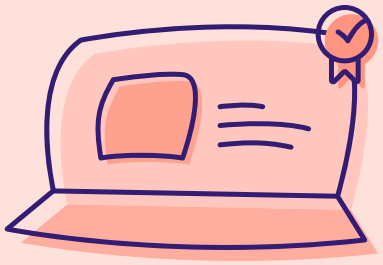
Qualio



The essential guide to life science supplier management

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The life science world is changing. The days of insular industry monoliths handling drug and device development completely in-house are over.

The industry is fragmenting: hundreds of ambitious niche start-ups and scale-ups are appearing, taking on specialized roles in ever-expanding and increasingly complex supply chains.

The future of the industry is collaborative, connected and decentralized. Needless to say, airtight supplier management is now more crucial than it's ever been.The more you outsource, the more the safety and efficacy of your product hinges on your supply chain tactics.

The average life science company now relies on about 600 suppliers. Moderna's COVID-19 vaccine needed over 3000. And supply chain disruptions are only increasing year-on-year.

Qualio doesn't only make software that gives life science companies complete supply chain control. We also think it's crucial to share the best practice, expertise and know-how that businesses need to avoid supply chain catastrophe, and to make themselves as proactive and protected as possible.

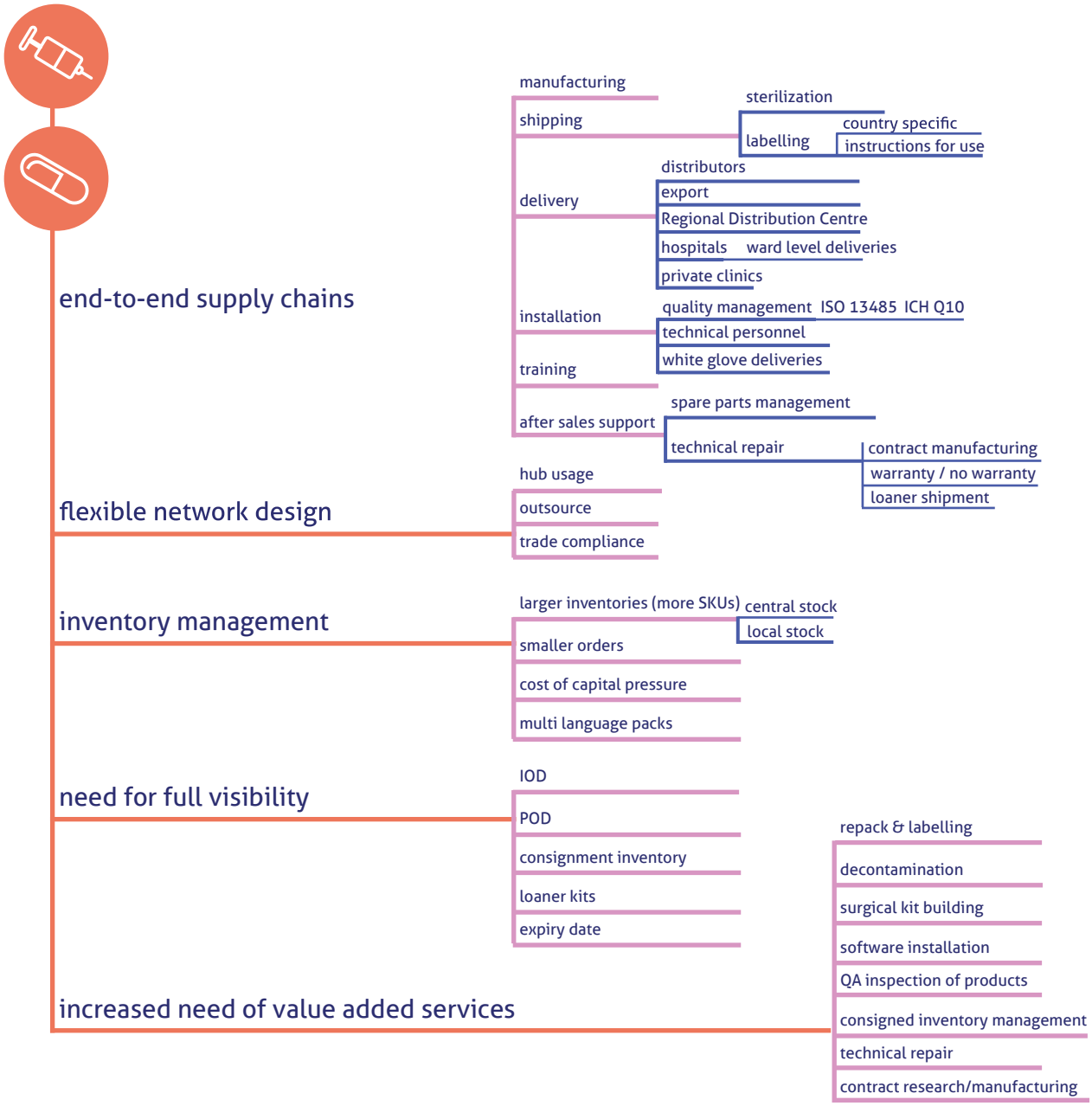
Your business is only as strong as its weakest link.

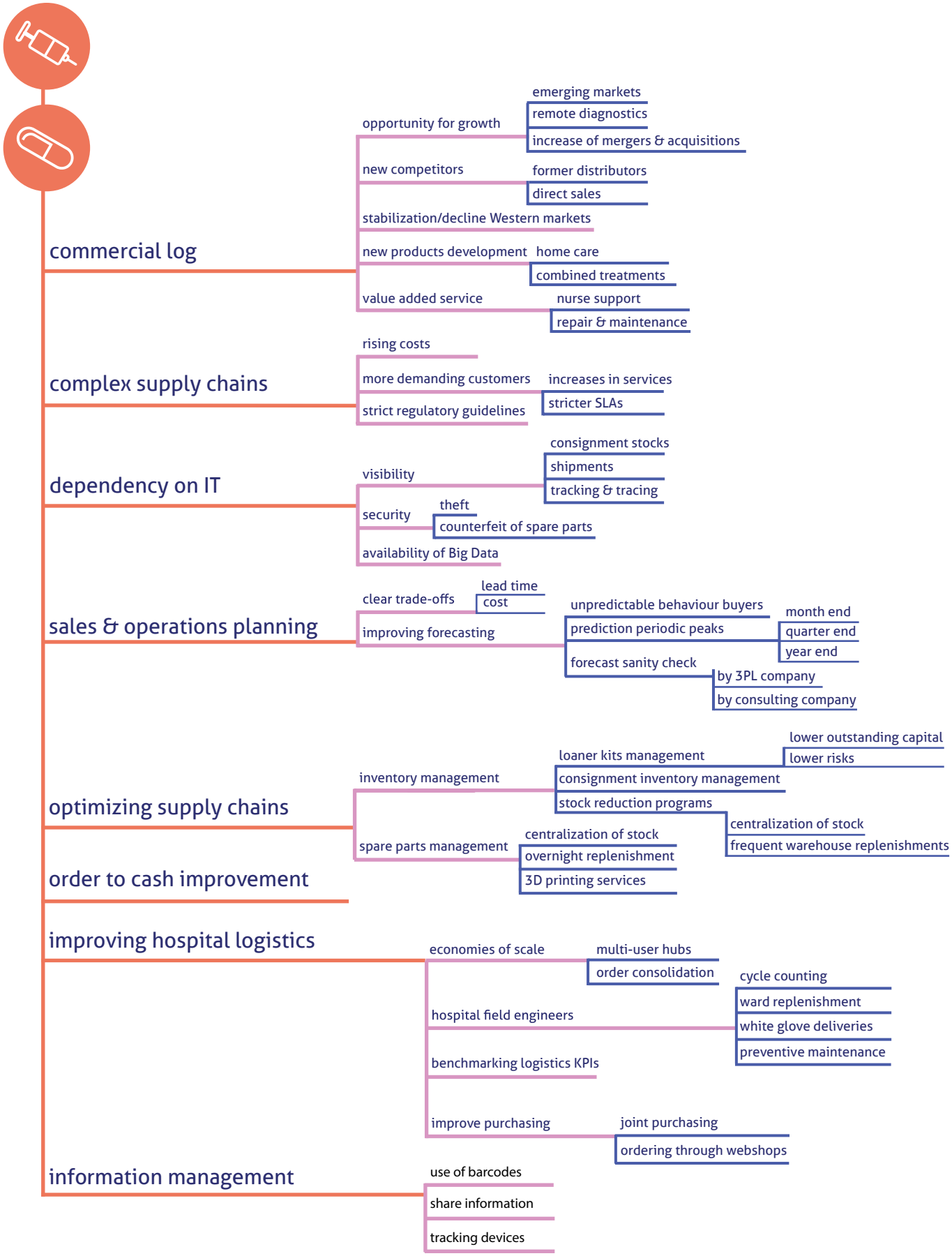
This guide is designed to make that weakest link as strong as it can be.

Meg Sinclair

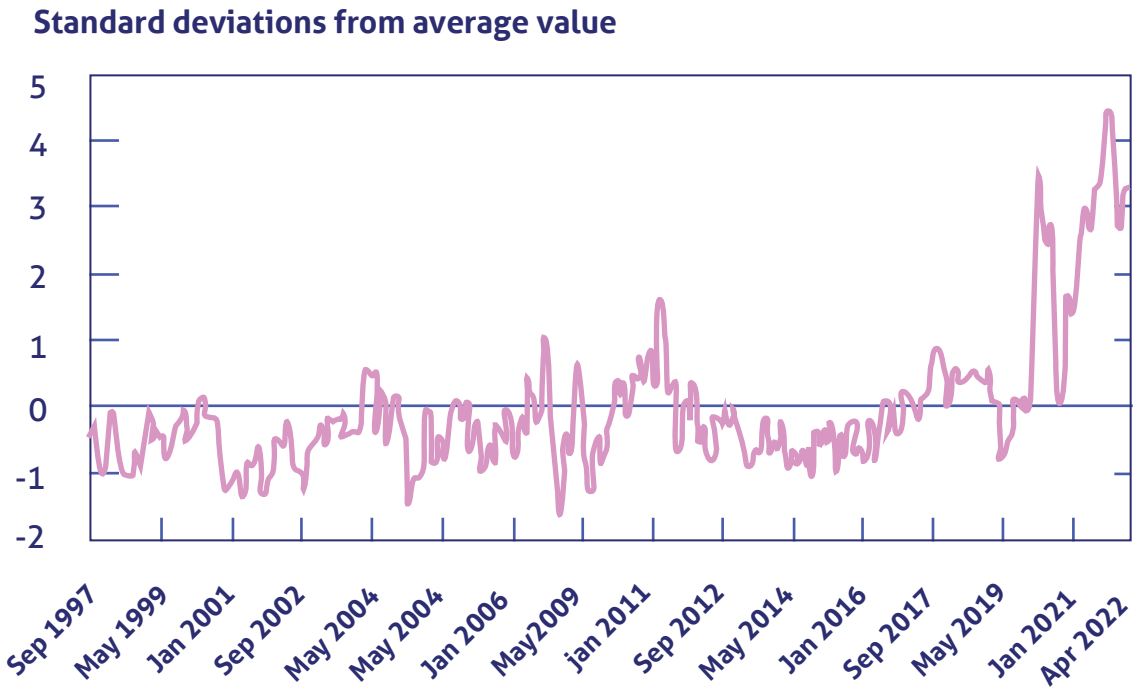
Senior Manager, Quality and Support

The modern life science supply chain: why is good supplier management so important?




commercial log
opportunity for growth
emerging markets
remote diagnostics
increase of mergers & acquisitions
new competitors
former distributors
direct sales
stabilization/decline Western markets
new products development
home care
combined treatments
value added service
nurse support
repair & maintenance
complex supply chains
rising costs
more demanding customers
increases in services
stricter SLAs
strict regulatory guidelines
dependency on IT
visibility
consignment stocks
shipments
tracking & tracing
security
theft
counterfeit of spare parts
availability of Big Data
sales & operations planning
clear trade-offs
lead time
cost
improving forecasting
unpredictable behaviour buyers
prediction periodic peaks
month end
quarter end
year end
forecast sanity check
by 3PL company
by consulting company
optimizing supply chains
inventory management
loaner kits management
lower outstanding capital
lower risks
consignment inventory management
stock reduction programs
centralization of stock
frequent warehouse replenishments
spare parts management
centralization of stock
overnight replenishment
3D printing services
order to cash improvement
improving hospital logistics
economies of scale
multi-user hubs
order consolidation
hospital field engineers
cycle counting
ward replenishment
white glove deliveries
preventive maintenance
benchmarking logistics KPIs
improve purchasing
joint purchasing
ordering through webshops
information management
use of barcodes
share information
tracking devices

Global supply chain pressure index



Life science supply chains face the most pressure and complexity in history. Life science businesses now rely on hundreds of interacting suppliers, around 10% of which are now fully virtual and remote.

Weak supplier management exposes your organization to the risk of multimillion-dollar recalls, reputational damage, fines, and even litigation and prison time.

Get it right, and your company unlocks a transparent, collaborative, risk-controlled and cost-effective pathway connecting your product to its target market.

7 top supply chain mistakes

1. Lack of fully binding quality agreements
2. Poor supplier-customer communication
3. One-size-fits-all supplier strategy
4. No on-site audits of key suppliers
5. Weak purchasing controls
6. Undiversified supply chains
7. Reliance on regulatory oversight: no independent verification

3 case studies

1

An Irish pharmaceutical company outsourced production of its intravitreal (in-eye) needle to a supplier. The supplier altered its manufacturing process without notifying them, since there was no specific clause in the two companies' quality agreement which would have forced them to.

Without full quality planning or oversight from the customer, the process change introduced a new risk of the product's silicon needle sleeve breaking off into a patient's eyeball during use. A multimillion-€ recall ensued.

2

A botox company had its needles sterilized by a third-party supplier. The supplier changed its sterilization process from radiation to a cheaper ethylene oxide gas without notifying. The two parties had no quality agreement at all in place. The sterilizing gas left a trace residue with the potential to contaminate biologics, affect product usage and cause cancer.

The customer was faced with both a heavy recall cost and the cost of sourcing a fresh supplier.

3

An American alcohol wipe manufacturer supplied GSK, Novartis, Pfizer, Bayer and others. They received numerous Form 483 observations across multiple audits, mainly for contamination risk. Yet their customers continued to work with them as a supplier. In the absence of a FDA warning letter, they didn't even perform an on-site audit.

The wipes were found to be contaminated with bacillus cereus after the death of a small boy in hospital for a routine operation. The wipe company was bankrupted and its owner convicted on felony charges, leaving the customers to face the liability and ensuing fallout.

What can we learn?

- Both supplier **and** customer are at fault
- Binding quality agreements could've stopped the first two events taking place by forcing the supplier to inform the customer of their process changes
- The alcohol wipe manufacturer should have had an on-site audit; any audit would've revealed dirty, contaminated pipes, bare-hand packing of 'sterile' product, under-staffing, unsuitable plant equipment, and staff who couldn't speak English (and therefore couldn't follow the QMS' documented SOPs!)
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- Customers didn't audit a highly dangerous supplier because they hadn't received a warning letter - so don't rely only on a lack of warning letters!
- Product liability lawyers will go after the name on the label – you! You are liable for a weak supply chain.

Key stat

15% of medical device Form 483s are caused by poor purchasing controls and non-compliance with 21 CFR 820.50

4 ingredients for airtight supplier management

1. Quality agreements (QAgs)

What is a quality agreement?

- Originally established for contract drug manufacture, but crucial for medical device supply chains too
- Binding written agreement between supplier and customer
- Not mandatory under FDA 21 CFR 211, but mandatory under EU GMPs Chapter 7, ICH Q7/Q10 and FDA 21 CFR 820.50

> *Complacency is not an option.*
>
> **— Anna Abram,**
> Deputy Commissioner for Policy, Planning, Legislation & Analysis, FDA

> *Contract manufacturers are an extension of [your] own facility.*
>
> **— FDA 21 CFR 200.100**

Quality agreements let you be the gatekeeper

You are the gatekeeper of all the services and goods received from your suppliers: ingredients, containers, parts, accessories, distribution, sterilization, manufacturing.

Your quality agreement is the key to the gate. Failure to meet the agreement? Gate locked!

Your quality agreements should:

1. Be unambiguous
2. Clearly map roles and responsibilities
3. Set mandatory information exchange
4. Set clear deliverables and timeframes
5. Have clear definitions for all content

Follow the Part 211 structure to ensure nothing's missed!

1. General
2. Organization & personnel
3. Buildings & facilities
4. Control of components
5. Production & process control
6. Packaging & labeling
7. Holding & distribution
8. Laboratory controls
9. Records & reports
10. Returned product / complaints

2. Audits

Give yourself a 'right to audit' clause

"[The supplier] will keep accurate and complete records.

[Your company] may audit [the supplier] relating to its performance under the terms of the quality agreement..."

What triggers a supplier audit?

1. Performance anomalies/SLA failure
2. Regulatory guidance
3. Patient/customer/regulatory feedback
4. Other clients of the same supplier
5. The calendar! Risk-based audit cadence if it's a critical supplier

Follow the Part 211 structure to ensure nothing's missed!

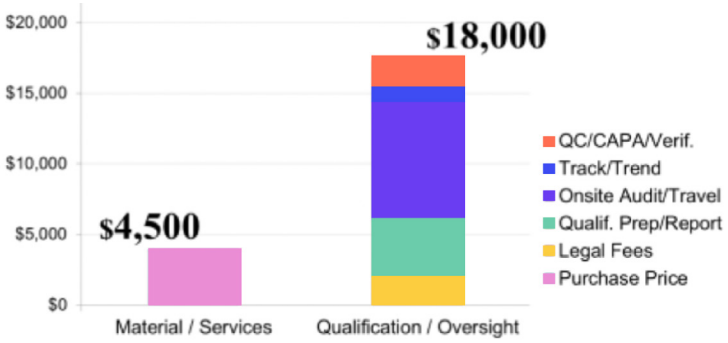
1. Pinpoint risks
2. Prove a functional QMS is in place
3. Document supplier relationships
4. Foster communication and trust
5. Strengthen your supply chain
6. Cut costs with preventive actions
7. Send the right message
8. Give suppliers improvement opportunities
9. Enforce transparency and honesty
10. Give yourself improvement ideas

Three reasons for risk-based supplier audits

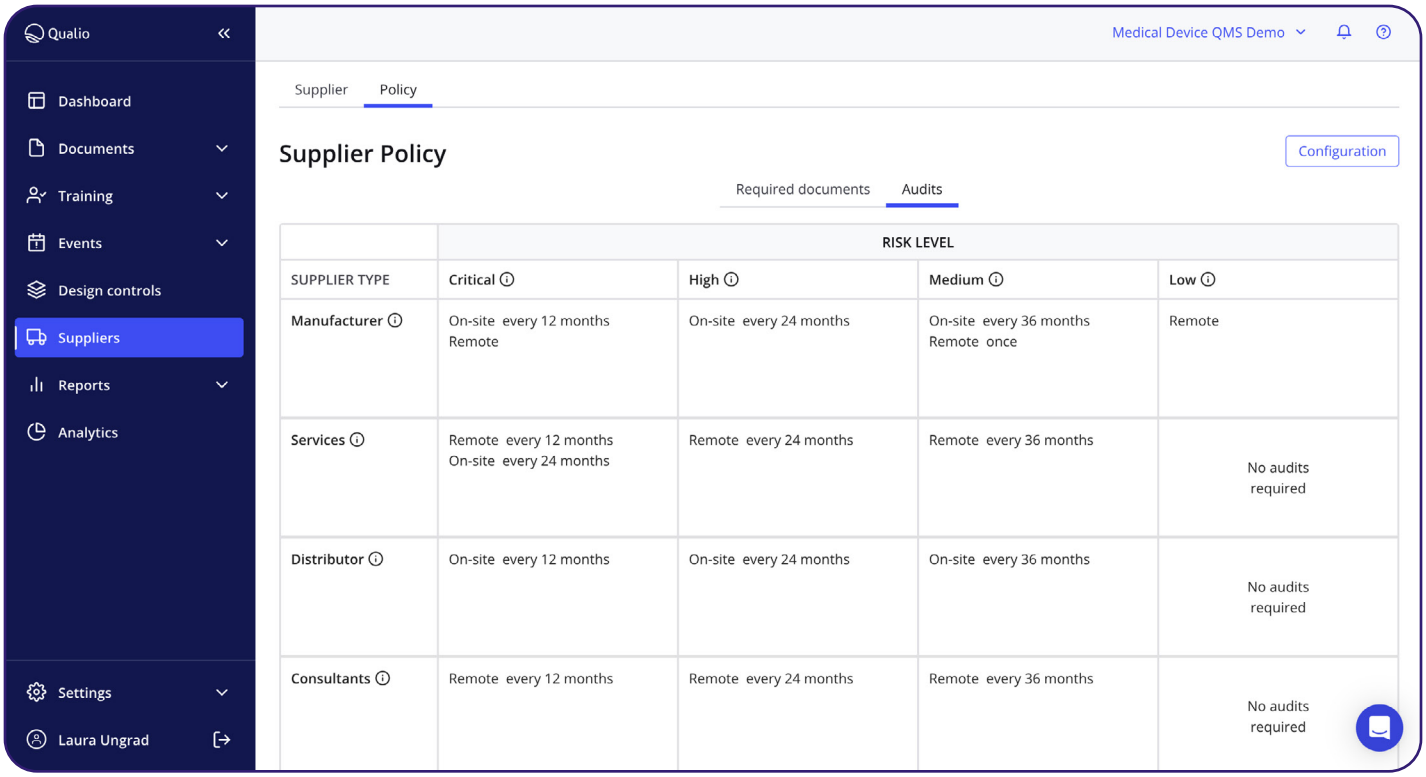
1. Focused efforts proportionate to supplier risk profile (there's probably no need to audit minor, low-risk vendors!)
2. Be more cost-effective
3. Perform fewer, higher-quality and more incisive audits

> *"You can audit anything, but you shouldn't audit everything. There's no point focusing on the molehill when there's a mountain."*
>
> **— Richard Chambers,**
> CEO, IIA

Complete oversight is impossible: pick your battles



Source: Cerulean Associates LLC



Here we can see how your supplier policy, in this case a digital matrix managed in Qualio Suppliers, should provide a risk-based audit requirements structure for your different supplier groups. For instance, you wouldn't waste your time auditing a low-risk consultant. A high-risk service provider, on the other hand, might need a remote audit every 2 years, while a critical distributor demands an annual on-site audit.

Suppliers should never be scored on a 'pass/fail' binary. Grading a supplier as 'satisfactory' or something similar could cause confrontations if something were to go wrong. Risk will always be present – no supplier is perfect. Your scoring needs to reflect that fact, as we can see in the blue box here.

Risk factors

Operational

- Product complexity
- Supplier location
- Quality data: complaints, NCRs, recalls
- Lone vendor or diversified?

Reputational

- Response to audit findings
- Public visibility of product
- Impact of supplier error(s)

Regulatory

- Audit histories
- Inspection histories
- Third-party regulatory conclusions (certification? findings?)

Financial

- Money spent with supplier (contract size)
- Liquidity/stability
- Likelihood/impact of disruption

Other risks to consider

Growth

If your supplier is expanding rapidly, can they keep up with demand?

Are they adequately staffed?

IT systems

Is their QMS manual and paper-based, slowing processes and increasing the risk of information loss or disconnect?

Are they embracing modern quality management tools like an eQMS?

Facility changes

Is new equipment being added? Will any processes need to change?

Chain length

How far from your business does your chain stretch?

Do you have insight of your supplier's suppliers?

Top tip

Treat your suppliers like a stock portfolio. Diversify and give yourself 2+ suppliers for key parts, components, services, etc. Choose a preferred supplier and a back-up and split orders to maintain minimum order volumes with your back-up.

Onboard with care

Pre-audit

1. Research
2. Set your standards
3. Focus
4. Choose carefully with maximum data

Mid-audit

1. Build a relationship
2. Foster an open, collaborative atmosphere
3. Tell the 'desired vs. actual' narrative
4. Use identified risks to determine if you want to work with them

5 due diligence areas for onboarding

Website

- Professional appearance
- Consistent info
- No misspelling of regulatory terms
- Physical and email addresses match expectations

Ops

- Liability insurance
- Financial history
- Registered with relevant authority
- Shared language with you
- Industry focus
- Case studies/experience

Industry

- Accreditation and standards
- Industry body membership
- Awards
- Marketing content: whitepapers, resources
- Awards
- Third-party reports

History

- Google search, go 5 years back
- Litigation
- Recalls
- 483s
- Warning letters
- Disputes

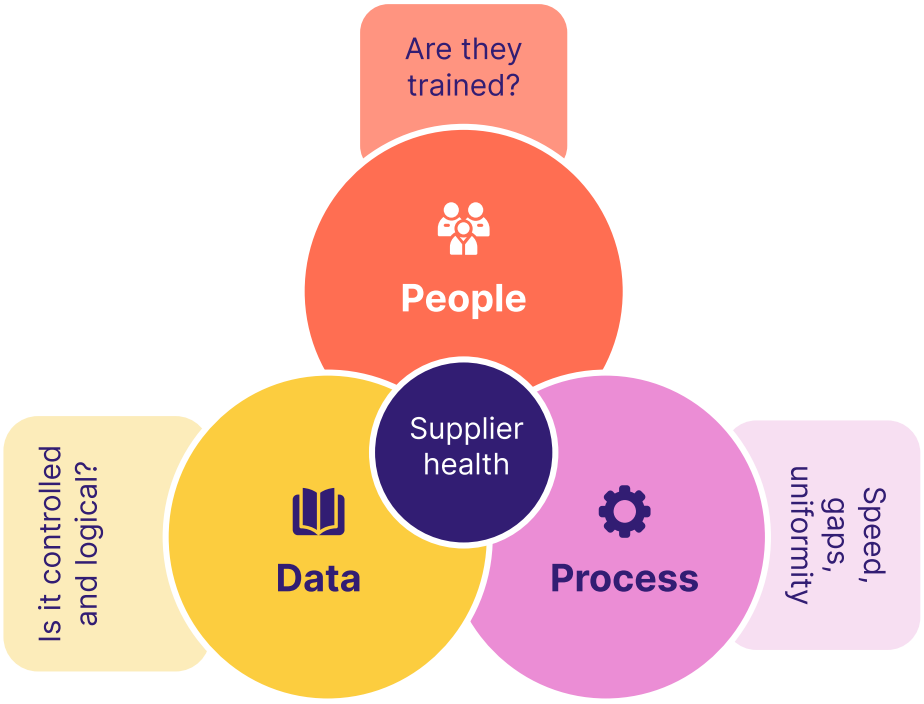
Remember: absence does not equal perfection!

Leadership

- Search individual execs
- Fraud
- Prison time
- Bankruptcy
- Investigations
- Public speaking
- Interviews and media

What to look for in a supplier audit

- General impression of the operation: ‘the vibes’
- Equipment, machinery, manufacturing, testing
- Internal and external comms
- Logistics and supply
- Site/product security
- Environment, health and safety (goods return/disposal)
- Employee competence and qualification
- QMS: documentation, match with reality
- Packaging
- Their own procurement/supplier management activity



Industry guidance for inspiration

- ISO 19011
- GHTF guidelines for medical device QMS auditing
- PIC/S pharmaceutical audit checklist
- WHO good manufacturing practices for biological products
- WHO good distribution practices for pharmaceutical products

Other industry guidance for inspiration


GHTF/SG4/N84:2010

GHTF

FINAL DOCUMENT

Global Harmonization Task Force

Title: Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers
Part 5: Audits of Manufacturer Control of Suppliers

Authoring Group: Study Group 4 of the Global Harmonization Task Force

Date: August 27, 2010

Dr. Larry Kelly, GHTF Chair

The document herein was produced by the Global Harmonization Task Force, which is comprised of representatives from medical device regulatory agencies and the regulated industry. The document is intended to provide non-binding guidance for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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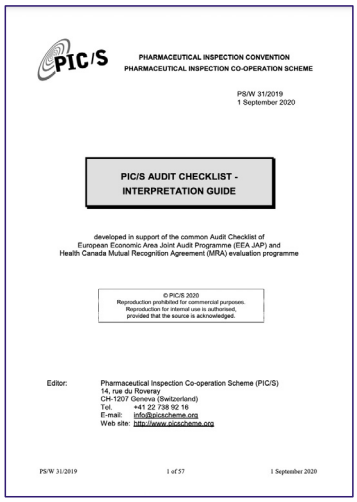
PIC/S

PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

PS/W 31/2019
1 September 2020

PIC/S AUDIT CHECKLIST - INTERPRETATION GUIDE

developed in support of the common Audit Checklist of European Economic Area Joint Audit Programme (EEA JAP) and Health Canada Mutual Recognition Agreement (MRA) evaluation programme

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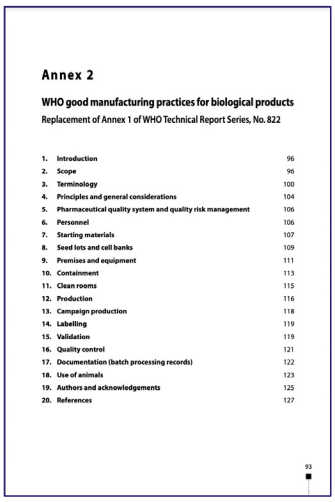
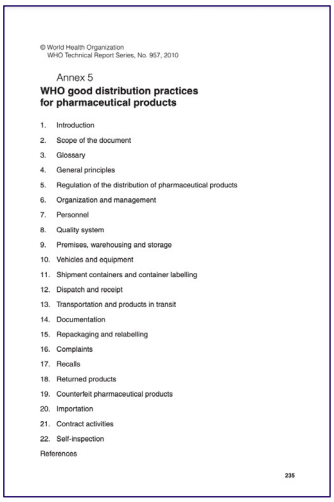

Annex 2

WHO good manufacturing practices for biological products

Replacement of Annex 1 of WHO Technical Report Series, No. 822



WHO Technical Report Series, No. 957, 2010

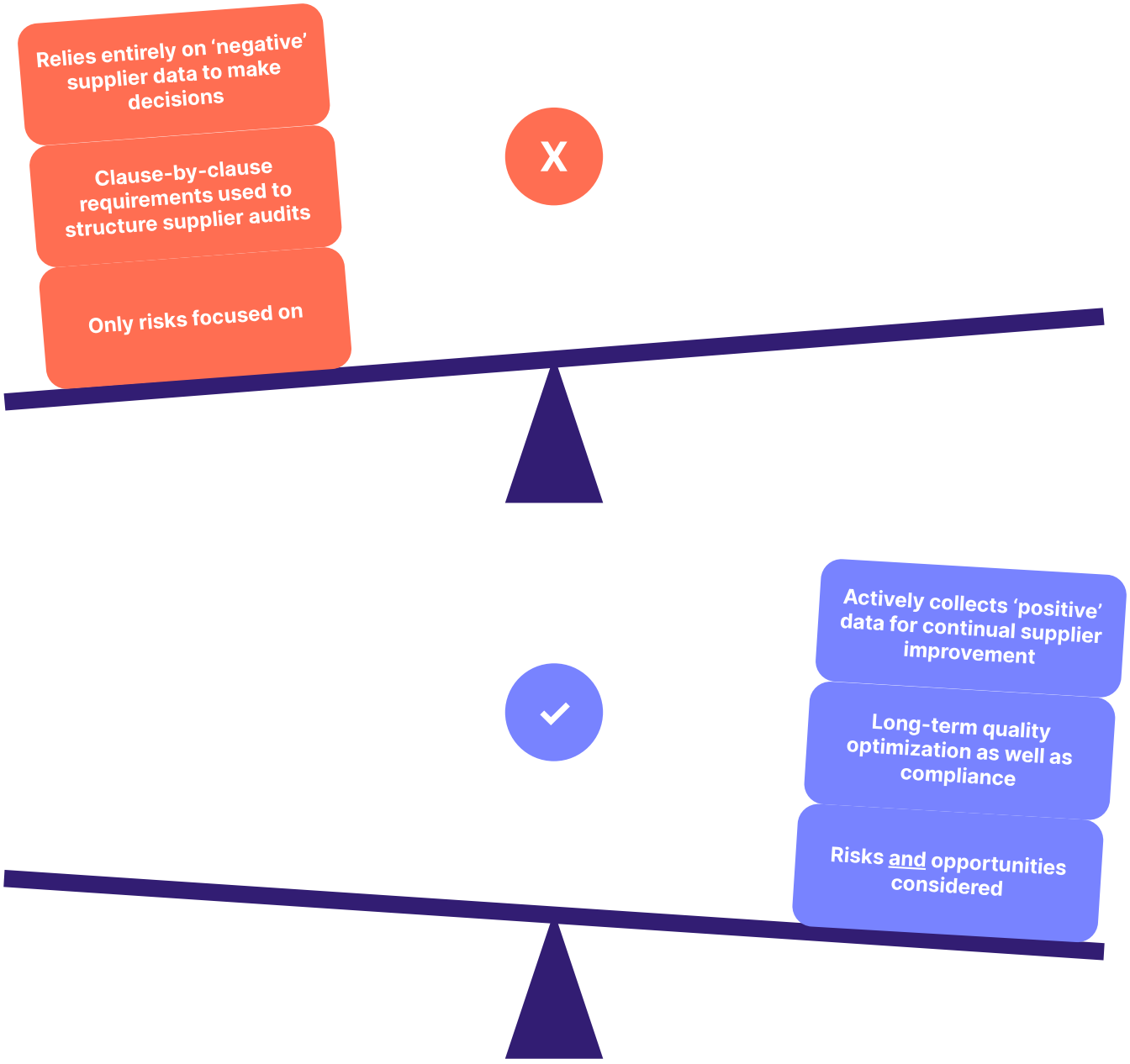
Annex 5

WHO good distribution practices for pharmaceutical products

Medical device

Pharma

Audit for quality, not compliance



Then what?

3. Metrics & data

An audit is your opportunity to set dedicated inspection time for a supplier. But there should be a constant 'bubbling' of background supplier data you can access in real time.

Qualification and monitoring is more than just auditing. Consider how you'll access constant supplier data sets like:

- Complaints: response times, underlying trends
- Quality agreement conformance
- CAPAs: completion, effectiveness, timeframes
- Change management: process updates and results
- Management review

Continuous metric visibility

Keeping a handful of key supplier metrics in your sights will let you keep your supply chain health under control and continuously improving. Consider metrics like:

On time in full (OTIF)

Fill rate

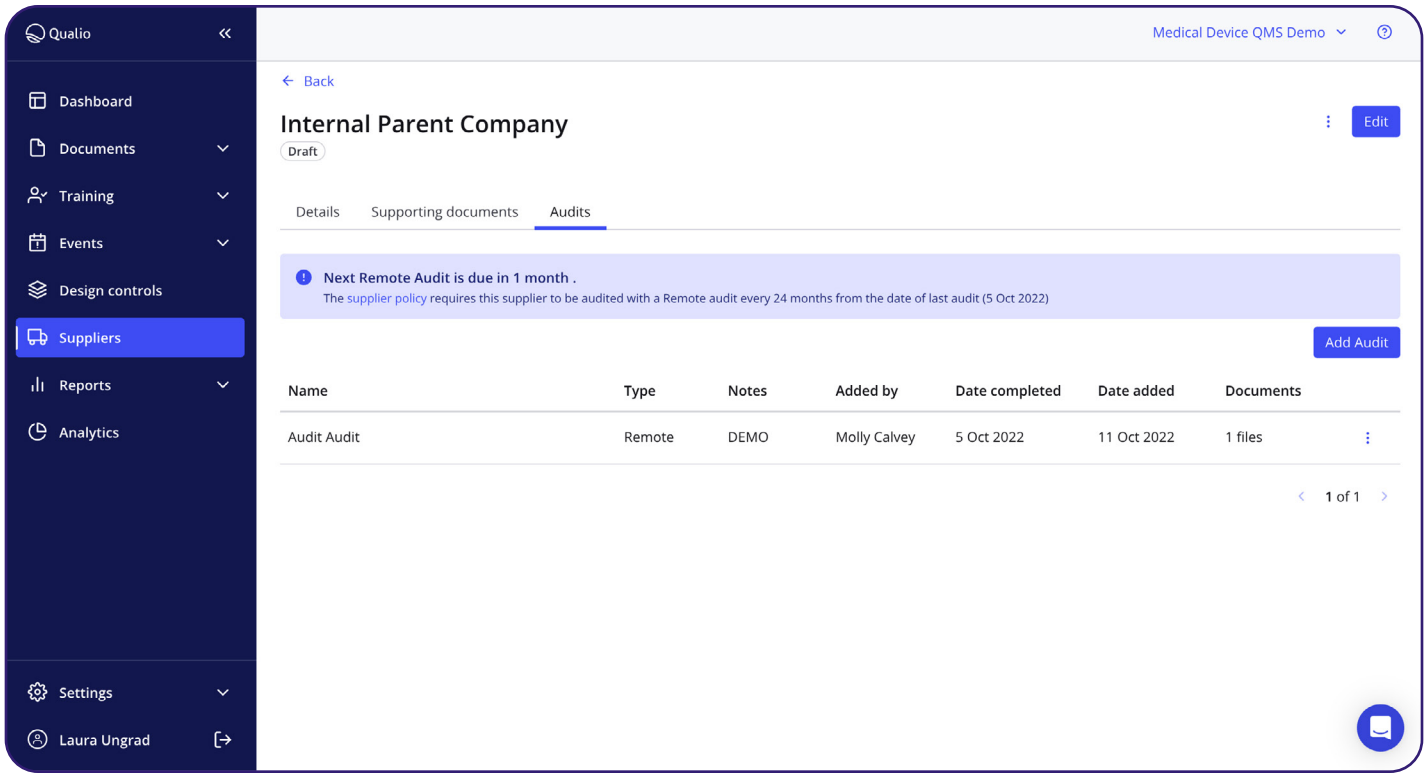
Days of inventory on-hand

Disposition on time

Supplier information you need to record

Initial	Long-term
1 Questionnaires	1 Ongoing audit reports
2 Due diligence records	2 Associated quality events: complaints, recalls, CAPAs
3 Qualification audit reports	3 Improvement plan (if needed)
4 Vendor certifications	4 Summary of key correspondence (don't rely on emails!)
5 Purchase order/contract/QAg	5 Risk levels/re-evaluations

Give yourself a mechanism for quick, easy supplier data access



4. SOPs

Last but not least, any robust supplier management system needs a set of strong standard operating procedures (SOPs) to structure and standardize your work. If you haven't already, develop SOPs for:

- General supplier management/purchasing controls policy
- Supplier selection
- Audits (remote and on-site)
- Quality agreements
- Continuous monitoring and evaluation
- Supplier dossiers and records

Qualio

See how Qualio gives you complete visibility of your supply chain

Schedule a demo with us