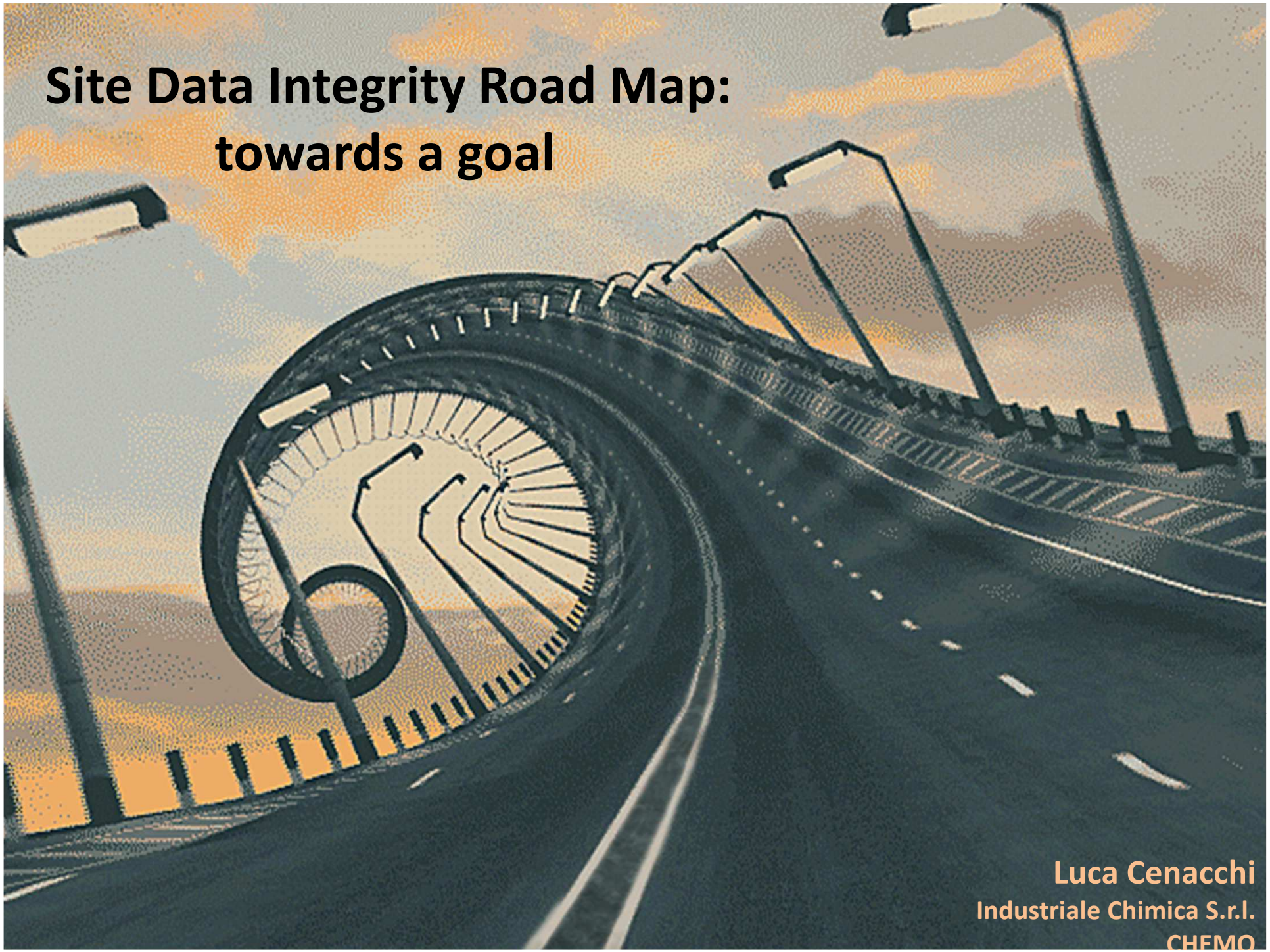
Site Data Integrity Road Map: towards a goal



Luca Cenacchi
Industriale Chimica S.r.l.
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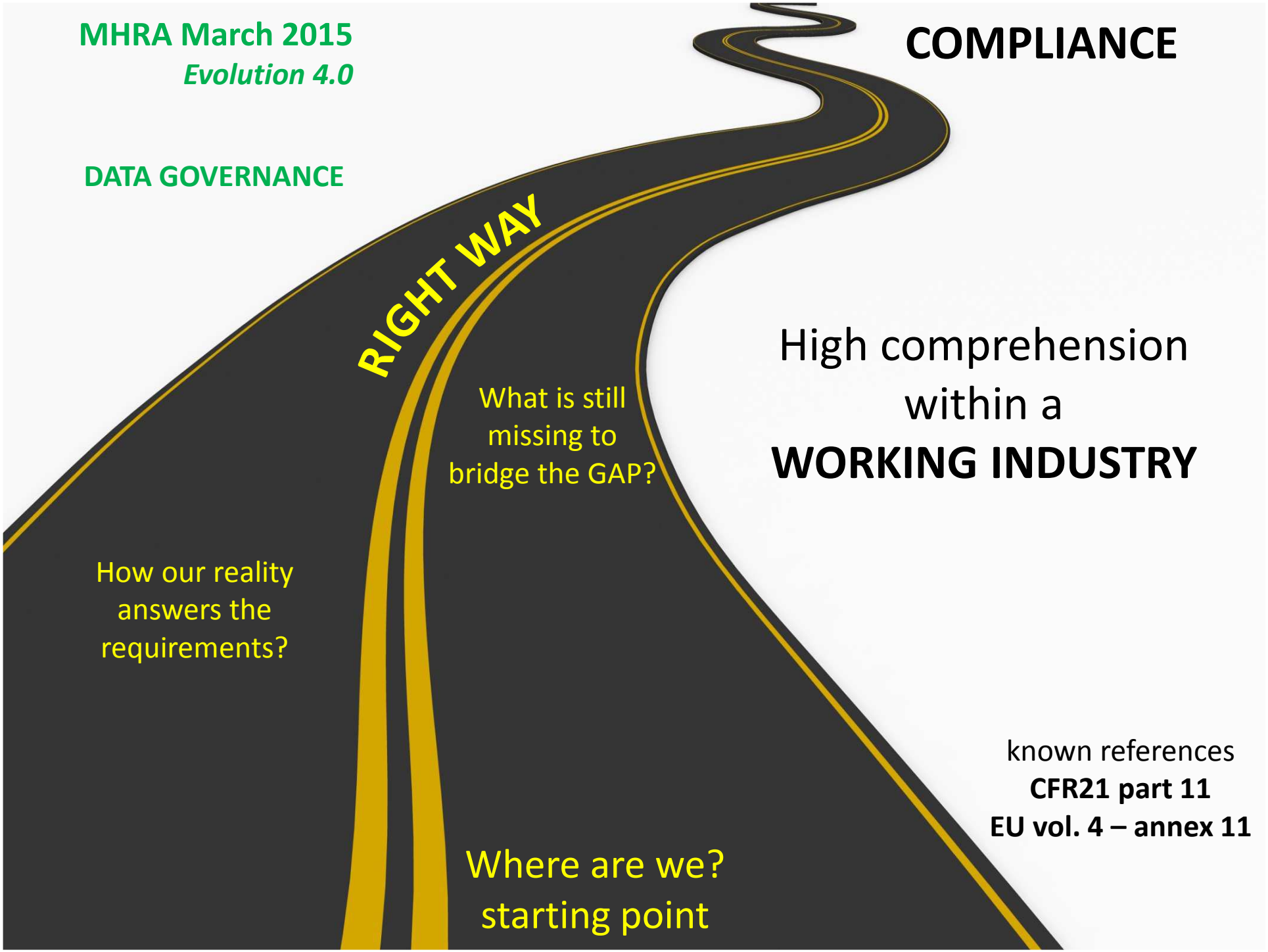
MHRA March 2015
Evolution 4.0
DATA GOVERNANCE
COMPLIANCE
RIGHT WAY
What is still missing to bridge the GAP?
How our reality answers the requirements?
Where are we? starting point
High comprehension within a
WORKING INDUSTRY
known references
CFR21 part 11
EU vol. 4 – annex 11

Medicines & Healthcare products Regulatory Agency

MHRA

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MHRA GxP Data Integrity Definitions and Guidance for Industry

Draft version for consultation July 2016

Organizations are not expected to implement a forensic approach to data checking on a routine basis, but instead **design and operate a fully documented system that provides an acceptable state of control based on the data integrity risk with supporting rationale**. In addition to routine data review, the wider data governance system should ensure that periodic audits are capable of detecting opportunities for data integrity failures within the company's system, e.g. **routine data review should consider the integrity of an individual data set**, whereas the **periodic system review might verify the effectiveness of existing control measures and consider the possibility of unauthorized activity**.

Data Governance

The sum total of arrangements to ensure that data, irrespective of the format in which it is generated, is recorded, processed, retained and used to ensure a complete, consistent and accurate record throughout the data lifecycle.

DATA ALTERATION & COUNTERFEITING

- Data modification, illegal and not traced
- Data deleting
- Data generation when it is not part of a documented and registered process

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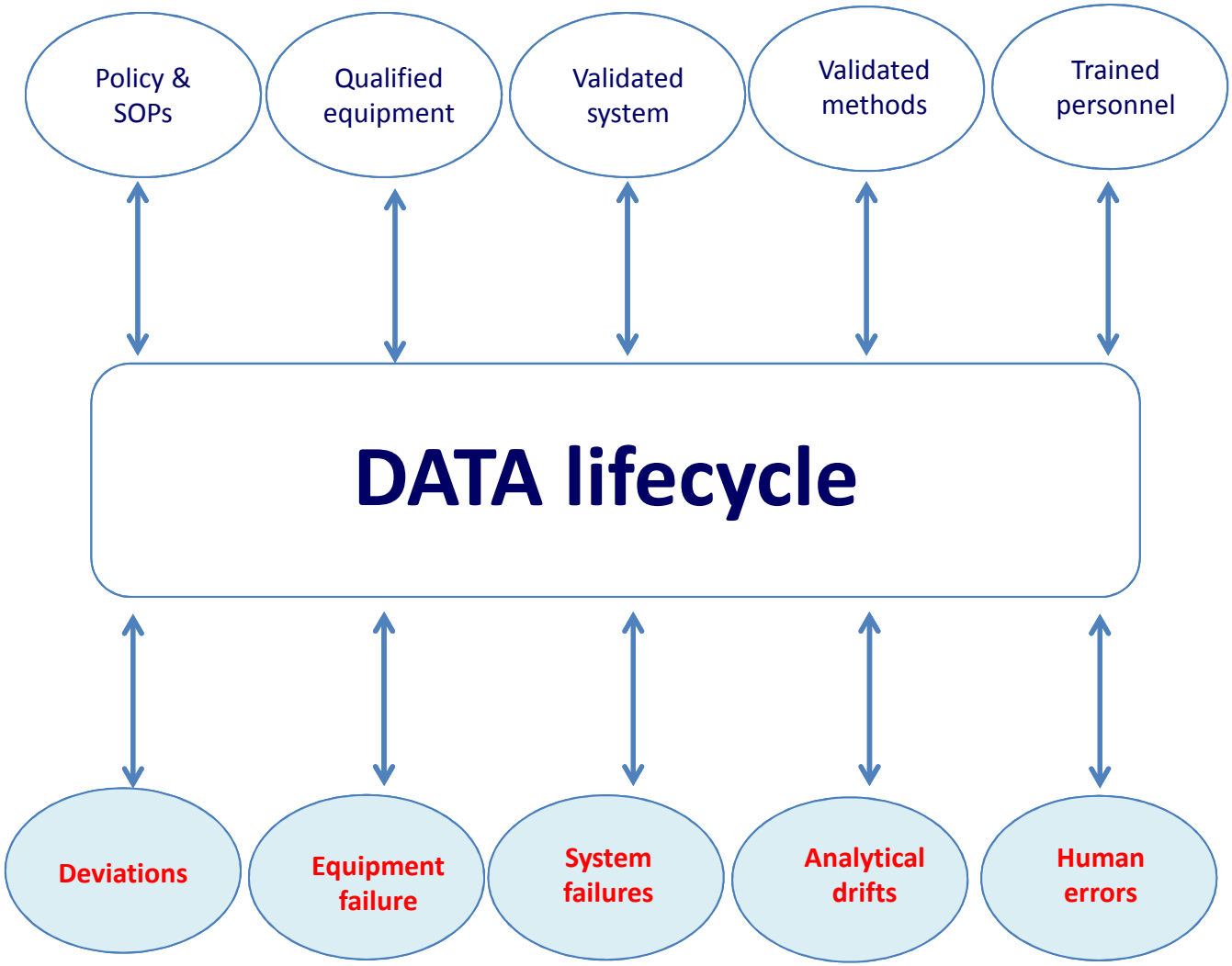

- DATA GOVERNANCE -

EU vol. 4 annex 11

Raw Data

Electronic & *Paper* records

MHRA March 2015

Metadata

STARTING POINT

a road map to perform a winning trip

A good roadmap of the trip, detailing the starting point and highlighting the stages to stop and perform a risk evaluation, it is recommended to **map the system**, trying to figure out a visual representation of the object of the study:

- facilitate the comprehension
- allow an organized analysis of systems, independently from their complexity
- identify the risks linked to the system
- facilitate the decisional processes
- facilitate the description of the system to “others”

A good choice is to proceed through key questions, applicable to each of the evaluated systems (whatever electronic or paper based and independently from the area) allowing to address appropriately **DATA INTEGRITY REQUIREMENTS** in terms of **CRITICALITY and TRACEABILITY of data**

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MAPPING the reality requires a deep understanding and analysis of complex systems, highlighting key points & drivers

WHAT

WHY

HOW

department	system ID #	software ID #	serial number	IT Administrator
IPC lab	HPLC-GC	EMPOWER	---	xxxxxxxxxxx
Release lab	BL01	no software	536N4010601	xxxxxxxxxxx
	GN 1	WINDOX SYMPATEC 5.60	1033/H1209	xxxxxxxxxxx
	IR 2	OMNIC 8.2	APW110075	xxxxxxxxxxx
	Granulometer	WINDOX SYMPATEC 5.60	1845/H1979	xxxxxxxxxxx
Production	Reactors	PLC7 siemens	AHY0900472	xxxxxxxxxxx
	Centrifuges			
	Drying /micronization			
QA	SOPs	DOCUMENTUM	AHY0900472	xxxxxxxxxxx
Warehouse	SAP			
	Wrack identification			
	Bar codes			
Engineering/ Maintenance	---	---	---	--
	---	--	--	

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… that is

➢ deep comprehension of the compliance requirements

➢ ability to read, identify and supervise when the achievement is assigned to third parties not directly belonging to our world

It means sharing different skills:

- **Analytical**
- **Engineering**
- **IT**
- **GMP**

with an accurate planning

INVENTORY

DEPARTMENT	CQ	PROD	QA	WAREH	ENG….	…..
SYSTEM IDENTIFICATION						
SOFTWARE						
INTERNAL CODE						
windows access						
software access						
access levels						
IQ						
OQ						
PQ						
acquisition						
storage/retrieval						
nomenclature						
path						
audit trail						
SOP						

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DEPARTMENT of APPLICATION	QC	QC	QC	QC	QC	QC
SYSTEM IDENTIFICATION	UV CARY 60	SHIMADZU IR-AFFINITY 1S	IR SHIMADZU	HPLC	METTLER SCALE AG135	METTLER SCALE MX5
SOFTWARE	Cary Win UV 5.0.0.999	LAB SOLUTION	IR EXPERT	DATASTORE A02.02	no software	no software
INTERNAL CODE	31	IR030	IR 9	HPLC1	scale1	scale2
windows access	Windows 7	Windows 7	Windows XP	Windows 7	not applicable	not applicable
software access	personal ID	personal ID	no	personal ID	2 levels id	2 levels id
access levels	2 access levels: Advanced User, Auditor; 3 profiles: Administrator, Audit, User	3 access levels: Adminsitrator Supervisor Analyst	none	5 levels: superadmin. or, superusers, users, readers, tech.	Admin, analyst	Admin, analyst
IQ	19/06/2016	29/05/2017	25/02/2013	42184	17/12/2003	14/07/2006
OQ yearly freq.	15/03/2017	29/05/2017	29/08/2016	14/06/2017 (HPLC-C)	28/06/2017	28/06/2017
PQ	28/07/2017	28/07/2017	28/07/2017	42944		
acquisition	local	local	local with network backup	network	printer	printer
storage/retrieval	local + backup	local	local	network	paper	paper
nomenclature	batch#	batch #.ispd	analysis n#.sws	yy-mm-dd.SC.SSI.zip	not applicable	not applicable
path	D:\Varian Spectroscopy Database	C:\labDB\DB\project_sequential number	C:\programs\shimadtzu\expert\run\myresults	OPENLAB DATASTORE\HPLC id-product\analysis year	not applicable	not applicable
audit trail	2 types: data + system	1 complete: data + system	none	2 types: data + system	not applicable	not applicable
SOP	SOP0109	SOP0123	SOP0116	SOP0128	SOP0113	SOP0113

Once the inventory is complete, the most difficult part of the way is over, we can proceed with specific tools through next steps

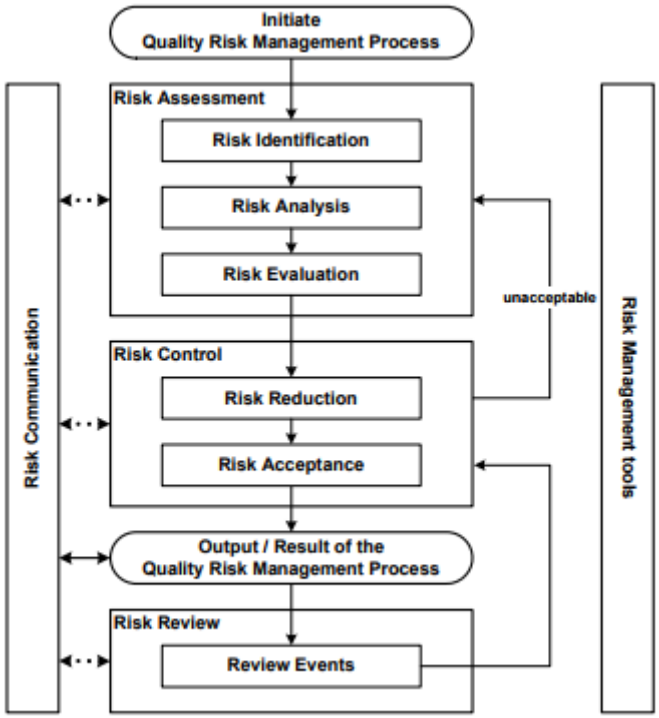
SECOND STEP

RISK ANALYSIS

ICH HARMONISED TRIPARTITE GUIDELINE

QUALITY RISK MANAGEMENT
Q9

- Basic risk management facilitation methods (flowcharts, check sheets etc.);
- Failure Mode Effects Analysis (FMEA);
- Failure Mode, Effects and Criticality Analysis (FMECA);
- Fault Tree Analysis (FTA);
- Hazard Analysis and Critical Control Points (HACCP);
- Hazard Operability Analysis (HAZOP);
- Preliminary Hazard Analysis (PHA);
- Risk ranking and filtering;
- Supporting statistical tools.



R (risk) = **T** (Traceability) **x C** (Criticality)

ALCOA (attributable, legible, contemporaneous, original, accurate) +
CCEA (complete, consistent, enduring, and available)

		CRITICALITY vs TRACEABILITY CRITICITA' vs TRACCIABILITA'	Number of negative answers		
CRITICALITY	CRITICITA'	Does the system generate data not used for release? *il sistema non genera un dato utilizzato per l'immissione in commercio della sostanza ?* Does the system identify who / when the data is generated? *il sistema identifica chi/cosa ha generato il dato?* Does the system generate attributable and permanent data? *il sistema produce informazioni leggibili e permanenti?* Does the system record simultaneously? *Il sistema registra il dato contemporaneamente alla sua generazione?* Does the system generate original data avoiding duplication? *Il sistema genera un dato originale evitandone la duplicazione?* Does the system generate accurate data? *Il sistema produce un dato preciso?*	(**No**) 5 - 6	**HIGH**	ALTA
			(**No**) 3 - 4	**MEDIUM**	MEDIA
			(**No**) 1 - 2	**LOW**	BASSA
TRACEABILITY	TRACCIABILITA'	Does the system have controlled and nominal accesses? *Il sistema ha la possibilità di accessi controllati e nominativi, protetti ?* Different users have different habilitations depending on the job? *a diverse utenze sono assegnabili diversi livelli di operabilità?* Are data saved and protected simultaneously to generation? *i dati sono salvati contestualmente alla generazione nel database e in formato protetto?* Is data saving automatic? *il salvataggio dati è automatico?* Can the system audit trail be challenged and cannot be switched off? *Il sistema ha un audit-trail interrogabile e non disattivabile?* Can electronic signatures and electronic data be traced and verified? *il sistema consente verifica e firma elettronica del dato?*	(**No**) 5 - 6	**HIGH**	ALTA
			(**No**) 3 - 4	**MEDIUM**	**MEDIA**
			(**No**) 1 - 2	**LOW**	BASSA

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	DEPARTMENT of APPLICATION	QC	QC	QC	QC	QC	QC
	SYSTEM IDENTIFICATION	UV CARY 60	SHIMADZU IR-AFFINITY 1S	IR SHIMADZU	HPLC	METTLER SCALE AG135	METTLER SCALE MX5
	SOFTWARE	Cary Win UV 5.0.0.999	LAB SOLUTION	IR EXPERT	DATASTORE A02.02	no software	no software
	INTERNAL CODE	31	IR030	IR9	HPLC1	Scale1	Scale2
CRITICALITY	Does the system generate data not used for release?	yes	yes	yes	yes	not applicable	not applicable
CRITICALITY	Does the system identify who / when the data is generated?	yes	yes	yes	yes	not applicable	not applicable
CRITICALITY	Does the system generate attributable and permanent data?	yes	yes	yes	yes	not applicable	not applicable
CRITICALITY	Does the system record simultaneously?	yes	yes	yes	yes	not applicable	not applicable
CRITICALITY	Does the system generate original data avoiding duplication?	yes	yes	no	yes	not applicable	not applicable
CRITICALITY	Does the system generate accurate data?	yes	yes	yes	yes	not applicable	not applicable
	CRITICALITY RISK INDEX	**LOW**	**LOW**	**MEDIUM**	**LOW**	**not applicable**	**not applicable**
TRACEABILITY	Does the system have controlled and nominal accesses?	yes	yes	no	yes	not applicable	not applicable
TRACEABILITY	Different users have different habilitations depending on the job?	yes	yes	no	yes	not applicable	not applicable
TRACEABILITY	Are data saved and protected simultaneously to generation?	yes	yes	yes	yes	not applicable	not applicable
TRACEABILITY	Is data saving automatic?	no	yes	yes	yes	not applicable	not applicable
TRACEABILITY	Can the system audit trail be challenged and cannot be switched off?	yes	yes	no	yes	not applicable	not applicable
TRACEABILITY	Can electronic signatures and electronic data be traced and verified?	yes	yes	no	yes	not applicable	not applicable
	TRACEABILITY RISK INDEX	**LOW**	**LOW**	**MEDIUM**	**LOW**	**not applicable**	**not applicable**

The detailed picture of the system and the methodology chosen allow to prioritize the actions, focusing & analyzing in details each specific GAP

THIRD STEP

GAP ANALYSIS

- INTERVENTION PRIORITY INDEX -

TRACEABILITY								
LOW	1	Low	Low	Low	Low	medium	medium
	2	Low	Low	Low	Low	medium	medium
MEDIUM	3	Low	Low	medium	medium	high	high
	4	Low	Low	medium	medium	high	high
HIGH	5	medium	medium	high	high	high	high
	6	medium	medium	high	high	high	high
		1	2	3	4	5	6
		LOW		MEDIUM		HIGH	
		CRITICALITY					

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EQUIPMENT CODE	UV31	IR030	IR 9	HPLC1	scale1
does the system generate data not used for release	yes	yes	yes	yes	not applicable
does the system identify who / when the data is generated	yes	yes	yes	yes	not applicable
does the system generate attributable and permanent data	yes	yes	yes	yes	not applicable
does the system record simultaneously	yes	yes	yes	yes	not applicable
does the system generate original data avoiding duplication	yes	yes	NO: to be replaced	yes	not applicable
does the system generate accurate data	yes	yes	yes	yes	not applicable
has the system controlled and nominal accesses	yes	yes	NO: to be replaced	yes	PARTIAL. Software should be implemented
different users have different URS,depending on the job	yes	yes	NO: to be replaced	yes	PARTIAL. Software should be implemented
data are saved and protected simultaneously to generation	yes	yes	yes	yes	not applicable
Is data saving automatic	PARTIAL: manual/logbook /training	yes	yes	yes	not applicable
the system audit trail can be challenged and cannot be switched off	yes	PARTIAL: the ADMIN can switch off but it remains traced	NO: to be replaced	yes	not applicable
electronic signatures and electronic data can be traced and verified	yes	yes	NO: to be replaced	si	not applicable

YES	The requirement is fulfilled
NO	The requirement is not fulfilled with no possibility to solve the issue
PARTIAL	The requirement is not fulfilled but through remediation actions the equipment will comply

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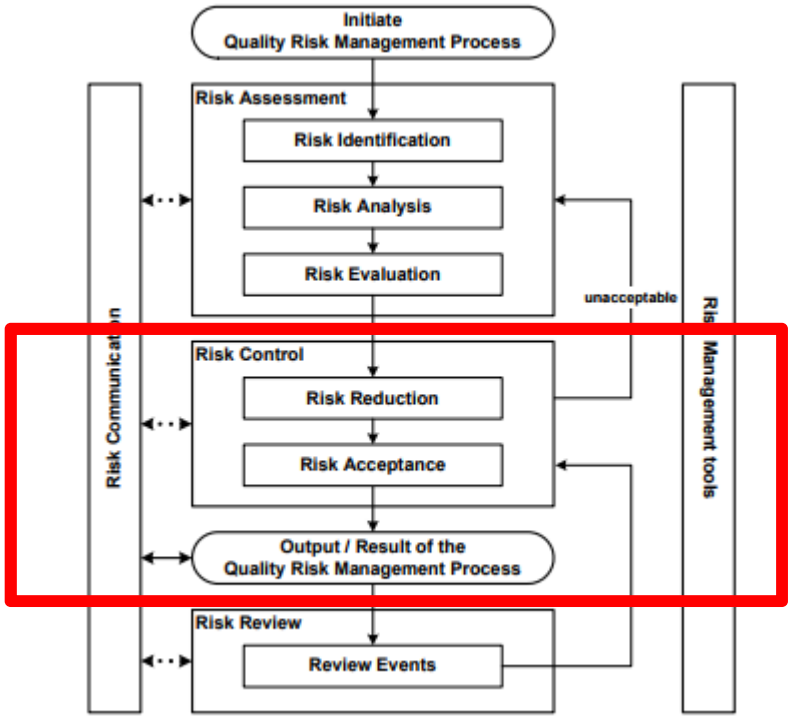
FINAL STEP

CAPA IMPLEMENTATION



Risk mitigation – REMEDIATION PLAN

All CAPA actions executed in the prioritization order driving each piece of the system into compliance

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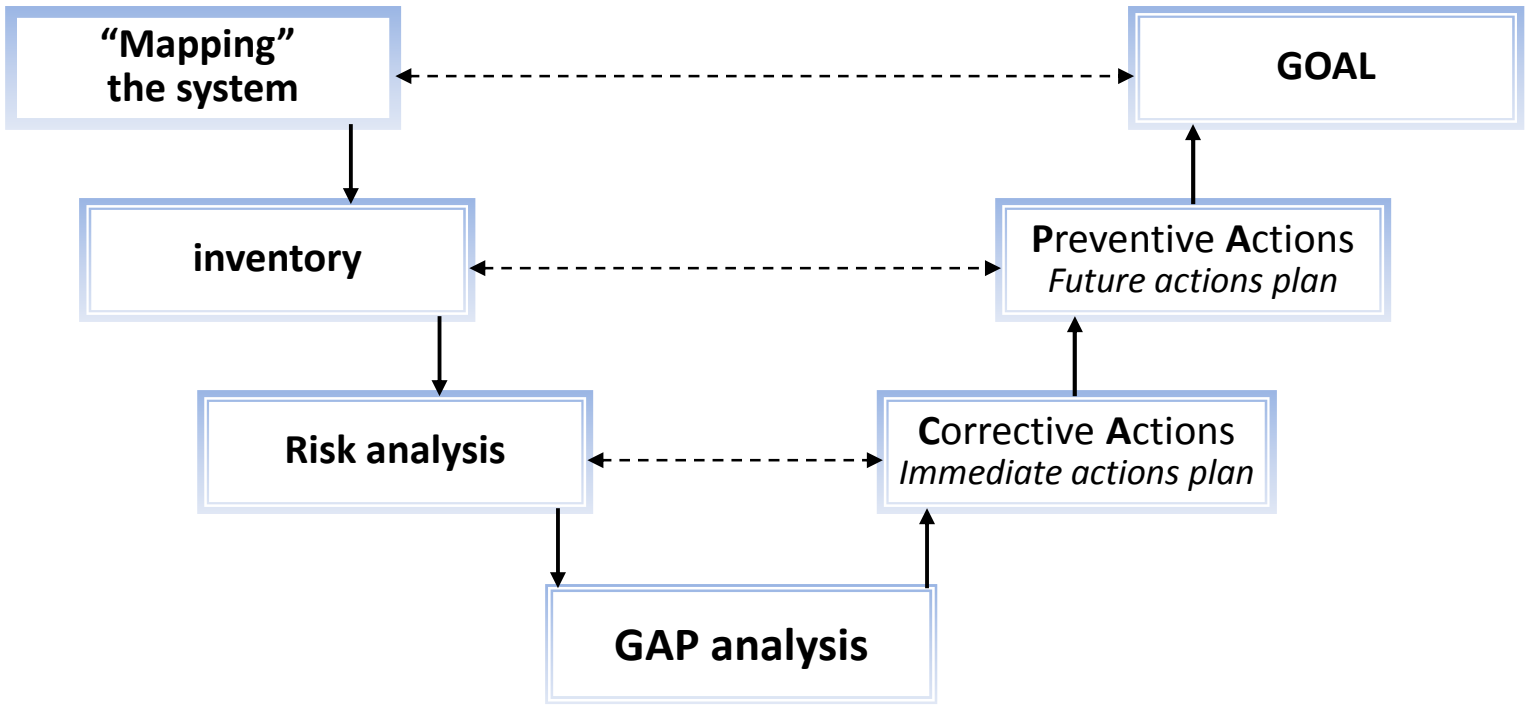
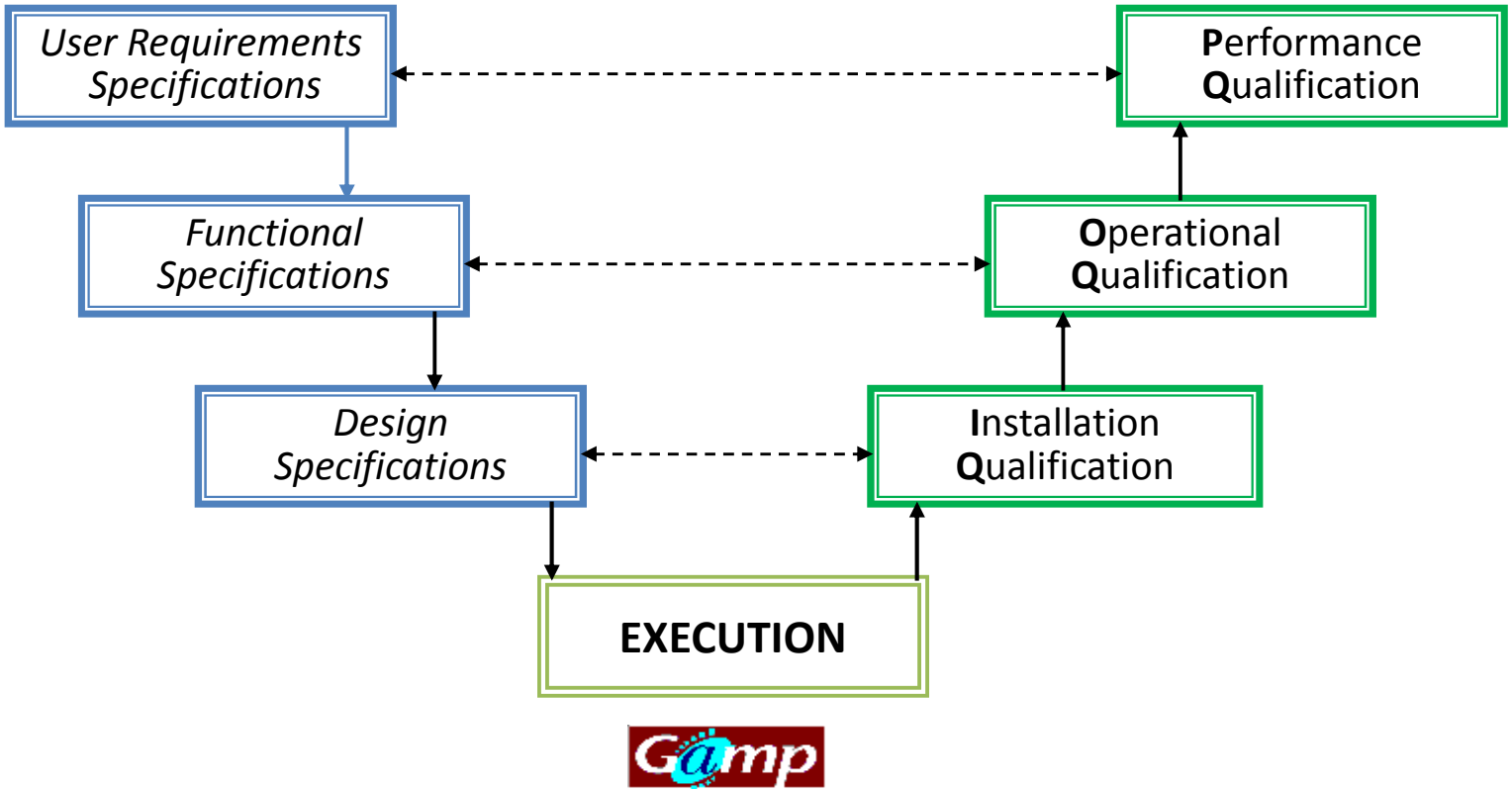
ROAD MAP
TRIP SUMMARY



Design VS Validation Process
(LIFE-CYCLE model)



One of the core principles of GAMP is that
Quality cannot be tested into a batch of product but must be built into each stage of the manufacturing process.

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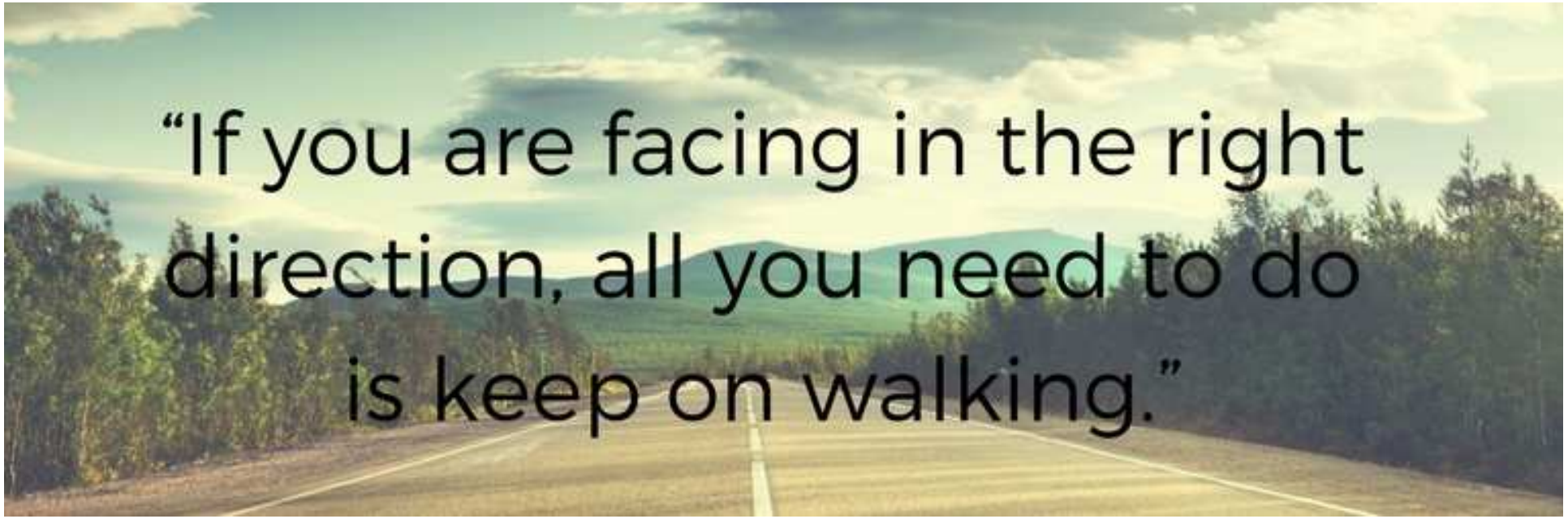

- Thank you for the attention -