



Life Science Consultants

Pharma 4.0

&

Smart patient reported outcomes

Connecting biology, physics and digital
For the benefit of human wellbeing

Nice to meet you!

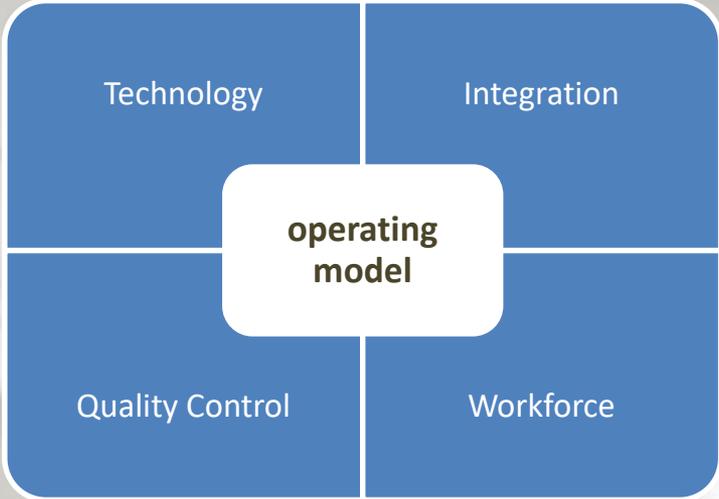
Hans.Heesakkers@Circuition.org

Is Managing Director of Circuition Life Science Consultants and Vice chair of ISPE Pharma 4.0
Brings a background of 30 years in the life science industry, 20 years in business process reengineering and IT projects,
15 years in manufacturing and supply chain management
and 15 years in the areas of clinical development and Investigational Products.



	Products	Services
Consulting	<p>Pharma 4.0 Scan The 4th industrial revolution as introduced by the world economic forum is meant to enable not only large, but also small and mid-cap companies! We can scan and report on your (sub-) organization to give direction to your organization's evolution.</p> <p>Empowered Value driven Organization Organizational restructuring that reduces the amount of hand offs and empowers staff to an extend where lead times are vastly reduced and quality improves. All guided by Consultants with a legacy in life sciences.</p>	<p>Project Management & Business Consulting We perform Project Management, Process and Requirements analysis and Change Management in the areas of Clinical Development, CMC development and Supply Chain Management. We love to cooperate with you as well as with other contractors.</p> <p>Validation coordination We are seasoned in Computer System Validation and well aware of regulations and guidances on CSV, Part 11/Annex 11 and data integrity. We can coordinate your projects executed by our offshore unit or executed by other contractors and use your SDLC and templates or ours.</p>
Software	<p>Clinical Collaboration Network An AI and Block chain-based IT platform for designing Clinical Supply Chains and integration of internal and external systems supporting your trial.</p> <p>ePRO+ A Multilingual Patient Diary System with extensive capabilities like written and spoken diary questions, e-Consent, Smart pack treatment adherence, temperature logging per kit, e-Notifications and e-Instructions.</p>	<p>Software Development Our offshore developers produce excellent software, mobile applications, interfaces and data migrations due to their long-term experience in developing GMP and GCP applications, while working under validation conventions. We are seasoned in high quality, cost worthy application services.</p> <p>Validation Execution Our offshore unit is regularly audited by Top 10 Life science companies and supports companies in the production and execution of maintainable validation scripts. We relieve your internal staff, so they can focus on operations.</p>





The 4 areas of any organization's operating model depreciate due to internal and external changes. This presentation explains how the latest technological developments, trigger new operating models in life science:
PHARMA 4.0

What is Pharma 4.0

what is

evolution

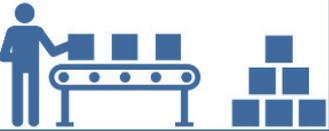
ePRO+



In the Life Science Industry we believe we are somewhat immune to hypes. Is Pharma 4.0 a hype?
What is Pharma 4.0?

What is Industry 4.0

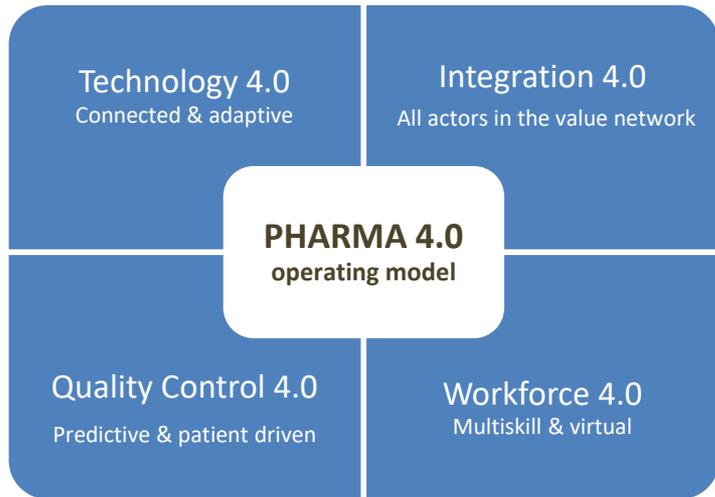
Is it a hype or a trend

				
Industry	1.0	2.0	3.0	4.0
Revolution	Steam power	Electricity	Computer electronics	Internet of Things
Evolution	Mechanization	Mass production	Automation	Cyber physical world

- Industry 4.0 is pushed by the World Economic Forum and many governments.
- Revolution sounds a bit scary and actually there was no industrial revolution but an industrial evolution at several moments in history.
- The trigger for these evolutions was a revolutionary invention though.
- Revolutionary in improving people's life so irreversible, that it triggered the industries to update their operating models.
- Most companies that didn't move up in evolution level historically either disappeared from the market, some survived by defining an exclusive niche.
- The "Internet of Things" is evolving with fast speed and global scale! The industry is responding with the 4th generation operating model.

What is Pharma 4.0

Evolving to a new operating model

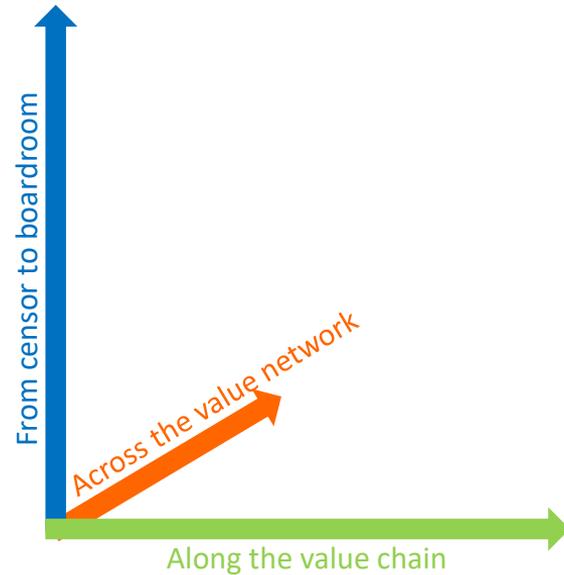


- The world population is becoming larger, older and with higher life expectancies!
- The era of block buster drugs is coming to an end!
- The life science industry needs to change its operating model to become adaptive to socio-demographic changes and scientific progress.
- Upgrading the operating model means evolving the four segments of an operating model:
 - Integration
 - Workforce
 - Quality Control and
 - Technology

What does a Pharma 4.0 operating model look like

Integration 4.0

Integration 4.0
All actors in the value network



3D Integration:

Reduce and automate hand overs in the value chain and in the hierarchy AND increase the number of exchanges in the value network

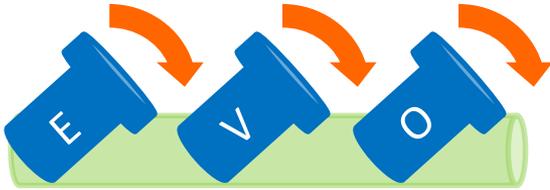
- From censor to boardroom
 - Real time data collection
 - Aggregated for different management levels
- Along the value chain
 - Minimizing hand overs in the process
 - Automating hand overs in the process
 - between internal AND external partners
- Across the value network
 - Handing over “in process” information
 - to other value chains “in process”
 - between development, manufacturing, health care market, clinical, science partners and finance.

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What does a Pharma 4.0 operating model look like

Work force 4.0

Workforce 4.0
Multiskill & virtual



EVO

A socio technical organization approach that turns the organization from functional to process and establishes information flows that enable quick decision taking.

Empowered

- Decision hierarchies are lowered
- Operational teams are empowered and enabled to take decisions in real time

Value driven

- Dissolve functional organizations into cross functional teams
- Focused on delivering value to market instead of delivering a half product to the next department
- Demand driven quality & quantity targets

Organization

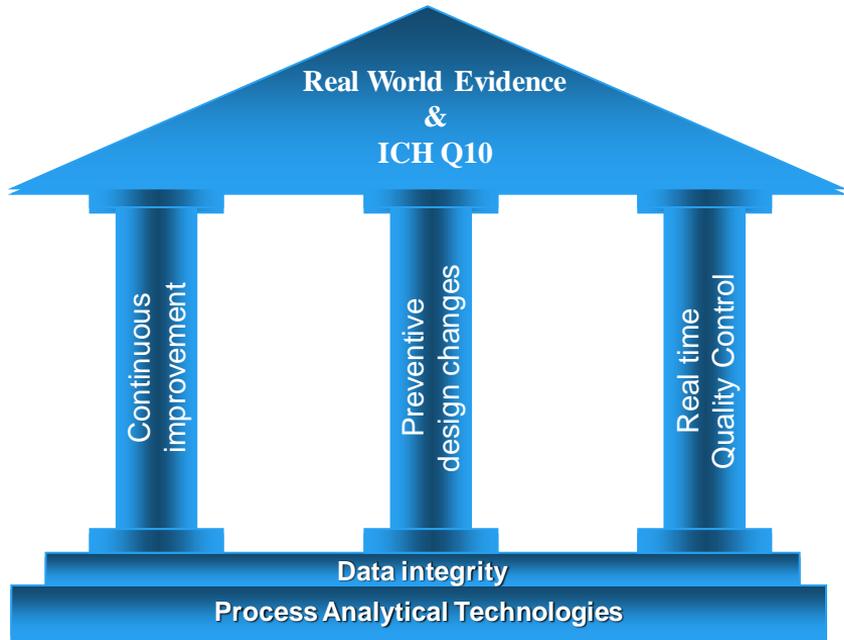
- Turn the organization structure 90°
- Virtual organizations (Geography and enterprise independent)
- Business and their IT partners are not separated

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What does a Pharma 4.0 operating model look like

Quality control 4.0

Quality Control 4.0
Predictive & patient driven



Continuous Quality Design

Enable improved versions of existing products by exchanges between development and manufacturing and replace product review/testing with process monitoring.

Continuous

- Feed back patient outcomes to development
- Establish Product Life Cycle Management.

Design

- Drive manufacturing issues to product and process improvements.

Quality

- Drive responsiveness over accountability.
- Replace product review/testing with automated analytical technologies

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What does a Pharma 4.0 operating model look like

Technology 4.0

Technology 4.0
Connected & adaptive



Internet of smart & robotic Things

Improve process quality and adaptivity by measuring all actors, transform that into information buckets throughout the value network and ensure equipment can quickly adapt to new products

- **SMART**
 - Distributed data capturing
 - Communication to different value networks
- **Collaboration networks**
 - Connecting software in the value network
 - Ensuring data integrity
- **Adaptive processing**
 - Handling large volumes efficiently
 - Quick adaption to product and process changes

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Evolution model

what is

evolution

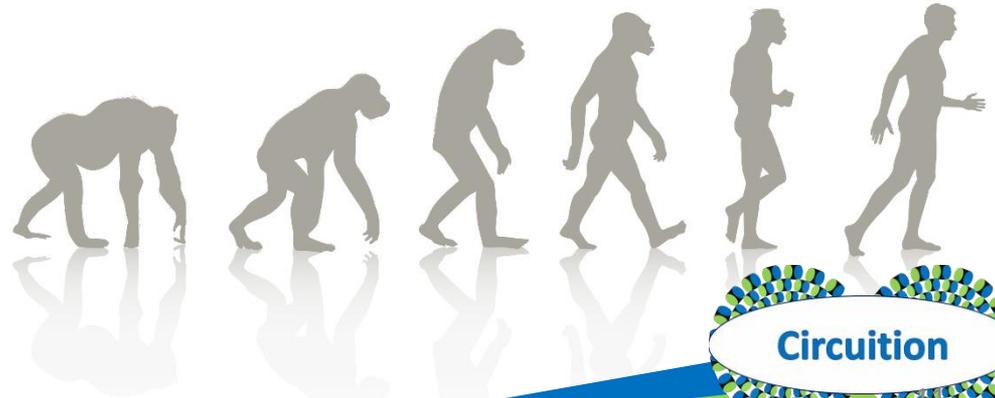
ePRO+

"It is not the strongest of the species that survive,
nor the most intelligent,
but the ones most responsive to change"
- Charles Darwin -

Pharma 4.0 is about responsiveness itself!

Big bang changes are not an option in our regulated world.

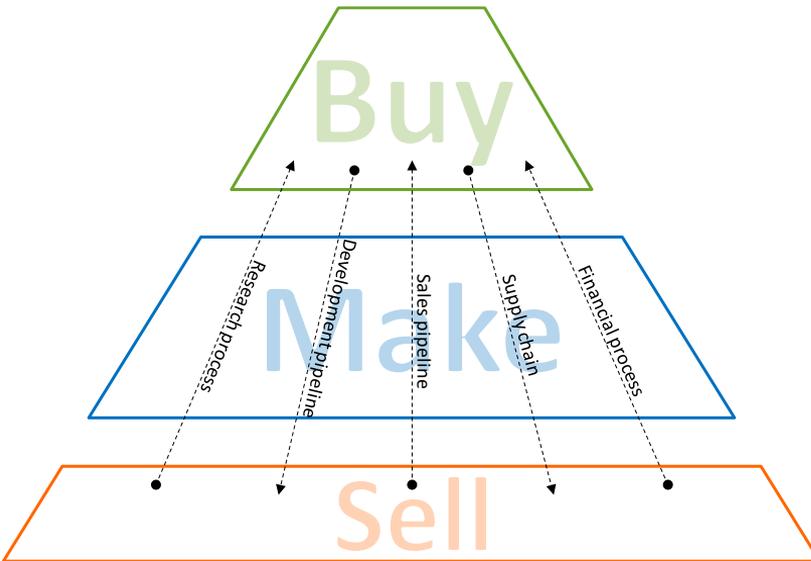
What does the evolution to Pharma 4.0 look like?



Evolution 1.0 to 4.0

Levels and evolutions

	1.0	2.0	3.0	4.0
Industry				
Change driver		Institutionalization	Computerization	Digitalization
Business driver		<ul style="list-style-type: none">• Need for efficiency• Increase of volume• Convince of Taylorism• Establish Production Management	<ul style="list-style-type: none">• Need to align with office processes• Increase of rules• Accept use of software• Establish Quality Control	<ul style="list-style-type: none">• Need for adaptiveness• Increase of market pull• Silo break down int&ext• Establish Data integrity• Continuously improve
Challenges				



Value network pictured by Circuition

Industry

- Different sub-organization in a value network can be at a different level of evolution
- A lower level sub-organization can impact the entire value network!

Business driver

- This is the result of business drivers being different for these sub-organizations.

Change driver

- A different business driver results in adoption of a different change driver

Challenges

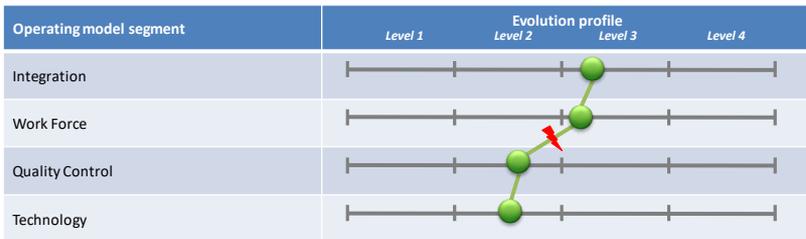
- Also the speed of change is depending on the agility of an organization to overcome challenges
- Furthermore the evolution level of an organization might have been impacted by merger into, or contracting to, organizations on a lower level

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Evolution 1.0 to 4.0

Levels within an operating model

				
Industry	1.0	2.0	3.0	4.0
Integration	Unit operation	Production Process	Supply chain	Value network
Work force	Craftmanship	Scientific management	Partial democracy	Virtual self organizing teams
Quality control	Product characteristics	Product & Process parameters	Balanced score cards	Driven by value network data
Technology	Mechanic	Electric	Computer electronic	Smart



Organization is held back by a „glass ceiling“



Organization is held back by a „lack of change management“

Operating model on the move

- Even within one organization the evolution level of the different operating model segments

– Integration

– Work force

– Quality Control

– Technology

might be on a different level

Capturing the business case

- This will result in value potential being created but not yet being captured
- An assessment (using score cards) of the organization helps to identify what is holding back the value capturing

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Reimbursement moves

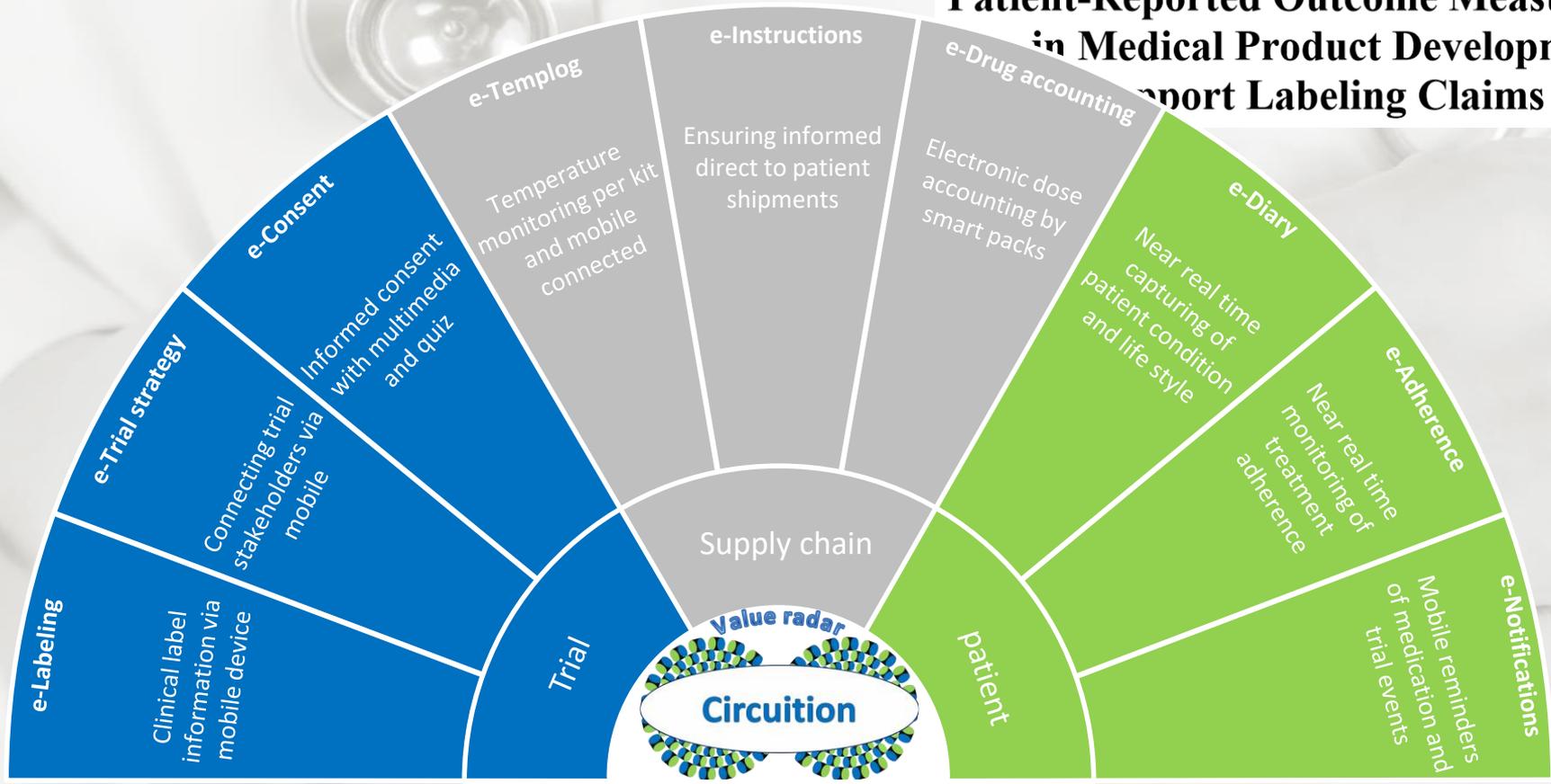
From “for treatment” to “for treatment outcome”

- How do we learn that outcome?
- How do we ensure treatment compliance?
- What is the effect of the patient’s life style?

e-PRO + Supply management

Value radar

Guidance for Industry Patient-Reported Outcome Measures: in Medical Product Development Support Labeling Claims

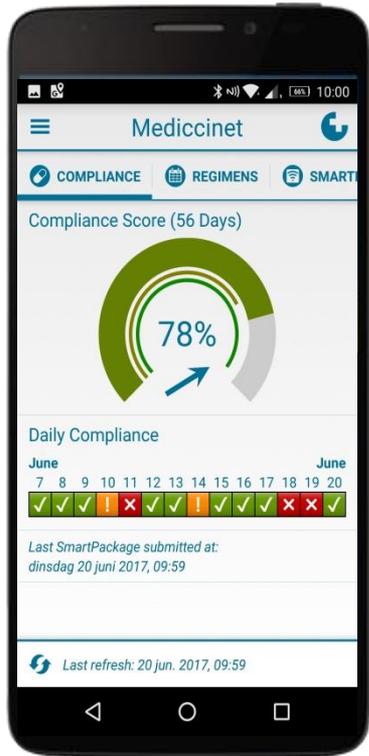


e-Adherence

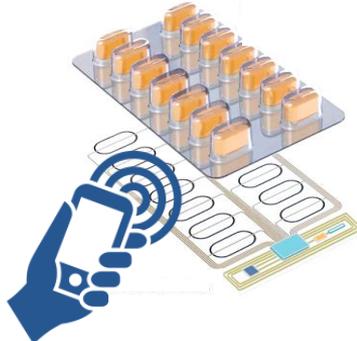
Value case



WHO research shows that poor adherence to treatment of chronic diseases is a worldwide problem of striking and still growing magnitude >50% of the patient population does not adhere to treatment schedules resulting in serious safety and efficacy issues Extrapolating the WHO figures to clinical trials, non-adherence will have a big impact on trial results and subject drop out Smart packages can trigger early and patient-safe responses to non-adherence



- Subjects in a trial are reminded to take medication in near real time
- Smart packs monitor if the right dose is taken at the right time
- Graphical feed back of adherence to subject itself
- Early notification of non-adherence to trial staff



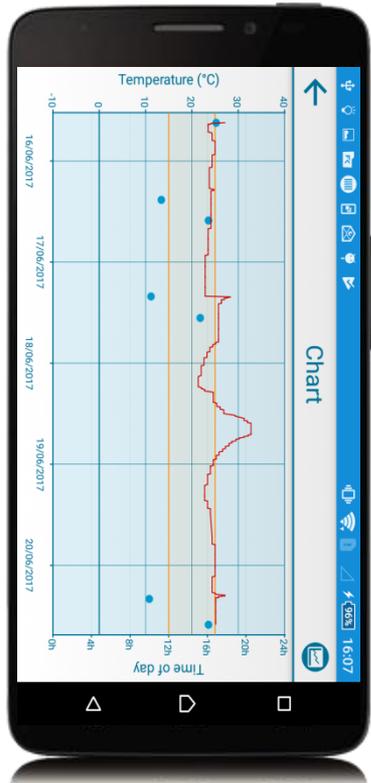


e-Templog

Value case



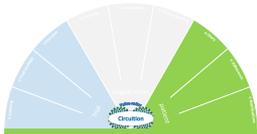
New regulations like the European GDP and the growing amount of trials with large molecules, trigger to improve the control of the temperature throughout the supply chain from formulation to patient. Traditional methods of temperature monitoring are limited to only parts of the supply chain and the visibility of excursions is limited to trial managers.



E-Trial medication with temperature chips enable:

- Temperature monitoring per kit
vs per shipper box
- Temperature monitoring for site and take home medication
vs for site medication only
- Near real time temperature log upload
vs event based upload only
- Visibility of temperature excursions to all parties in the supply chain
vs only to supply managers





e-Diary

Value case



A patient diary or PRO is any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else. Although the value of patient diaries is widely recognized, paper diaries suffer from "the parking lot effect" where patients forget to maintain the diary and fill it out just before their site visit. The use of multiple languages and multimedia further improves diary adherence. 📄



- Patient reported outcomes (PRO) or patient diaries
 - Show the patient's point of view
 - Monitor the condition of the patient
 - Enables to relate the patient condition to the treatment
 - Enables to relate the therapy result to the patient's life style
- ePRO is recommended over paper PRO because they
 - enable more reliable, smaller, faster, safer trials
 - prevent the "parking lot effect" by near real time data entry
 - trigger early responses to data queries



Let's shape the future of life sciences together!

Registered Trade Name of the contracting legal entity : Circuition BV

Registered seat of the company : Eindhoven, Netherlands

Registration number at the chamber of commerce : 64852245

VAT Registration number : NL855879245B01

Managing Director : JCM Heesakkers

Company Address : 't Heufke 11
5368 AZ Haren
Netherlands

Name, eMail and Telephone of your primary contact partner : Hans Heesakkers
E: hans.heesakkers@circuition.org
M: +31 654 642 648

Click below to learn more about our Pharma 4.0 offerings:

Pharma 4.0	
<u>Consultancy</u>	<u>Systems</u>
EVO	ePRO ⁺
Agile-CSV	Clinical Collaboration Network