



Circuition

Just in Time Labelling

After decades where label requirements
shaped the clinical supply chain
now the clinical supply chain
starts shaping label requirements

Business case

Business Case	In a nutshell	Key Concepts	Inner & Outer labels	
External Analysis				
Internal Analysis				
JIT strategy				

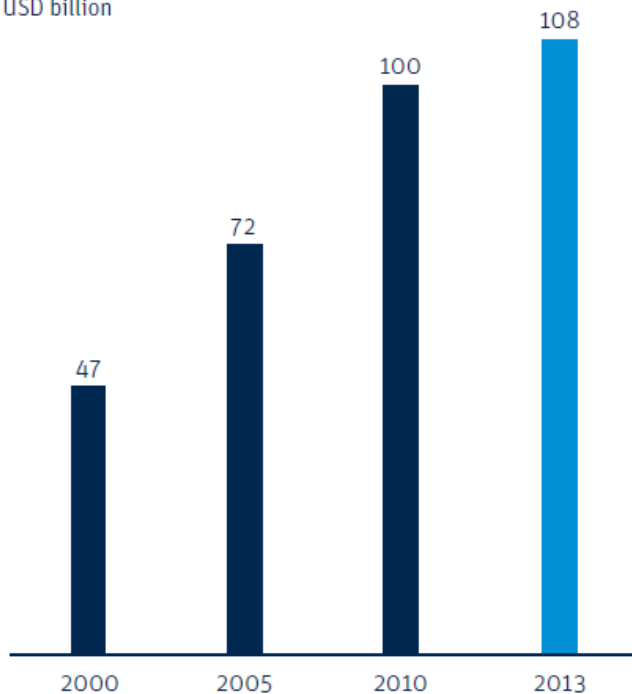
Business case

External analysis 1/8

Business Case	In a nutshell
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R&D expenditures
Worldwide

In USD billion



2013: provisional data
Source: EFPIA, PhRMA, vfa

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- **The total investment in Life Science R&D is increasing**
 - The worldwide Life Science R&D expenditure is still increasing
 - The amount of increase seems to decline
- The costs to develop a new drug is increasing
- A significant part of the costs is driven by clinical trials
- Within clinical trials the costs of phase 3 trial logistics is the largest driver

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Business case

External analysis 2/8

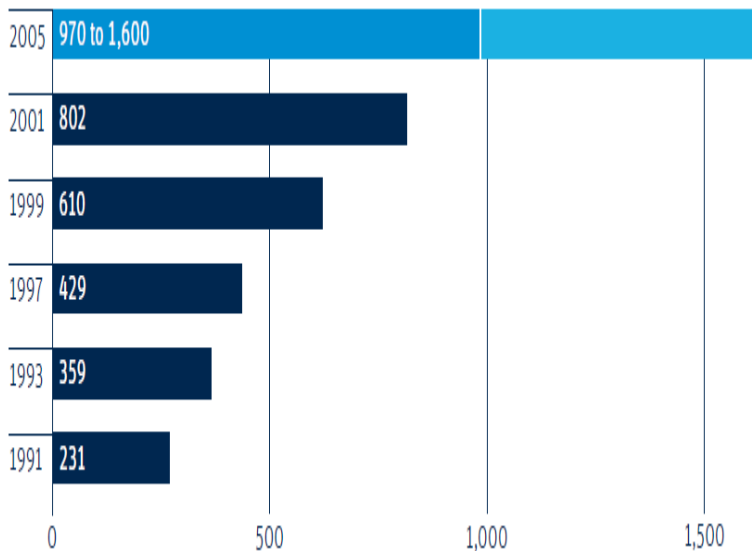
Business Case

In a nutshell

Key concepts

Inner & Outer labels

Development costs for a new pharmaceutical¹ In USD million



- The total investment in Life Science R&D is increasing
- The costs to develop a new drug is increasing
 - This increased expenditure is not due to an increased number of pharmaceuticals but due to an increased cost per developed pharmaceutical
- A significant part of the costs is driven by clinical trials
- Within clinical trials the costs of phase 3 trial logistics is the largest driver

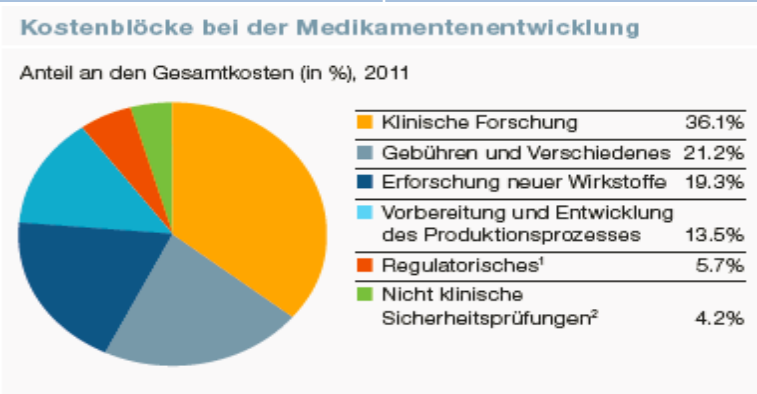
¹ Failures and costs of long-term capital commitment included

Sources: Di Masi J., et al., Tufts University (1991); Office of Technology Assessment (1993); Myers and Howe (1997); Office of Health Economics & Lehman Brothers (1999); Tufts University (2001); "The current state of innovation in the pharmaceutical industry" (Report for the European Commission, June 2008)

Business case

External analysis 3/8

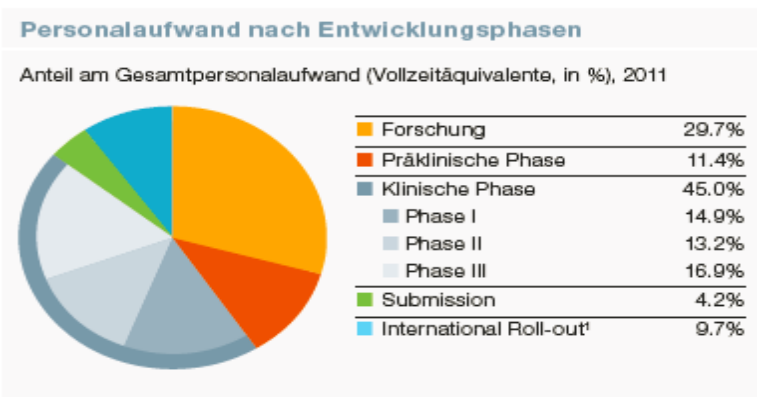
Business Case	In a nutshell	Key concepts	Inner & Outer labels	
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Quelle: CMR International, 2012 Pharmaceutical R&D Factbook, 2012.

¹ Kosten im Bereich Zulassung klinischer Studien, Marktzulassung, Patentfragen etc., ohne Gebühren.

² Zum Beispiel Toxizitätsprüfungen etc.



Quelle: CMR International, 2012 Pharmaceutical R&D Factbook, 2012.

¹ Phase nach der ersten Marktzulassung (Zugang zu anderen Märkten, Registrierungsgebühren etc.).

- The total investment in Life Science R&D is increasing
- The costs to develop a new drug is increasing
- **A significant part of the costs is driven by clinical trials**
 - Clinical trials remain the most expensive part of development
 - The costs of clinical trials define the amount of new pharmaceuticals that a LS company can push through her R&D pipeline
- Within clinical trials the costs of phase 3 trial logistics is the largest driver

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Business case

External analysis 4/8

Business Case

In a nutshell

Key concepts

Inner & Outer labels

More than half of the costs in 2005 were for clinical development, especially on logistically expensive, multinational phase III studies.

*Source: Statistics 2015,
Research based
pharmaceutical companies in Germany*

- The total investment in Life Science R&D is increasing
- The costs to develop a new drug is increasing
- A significant part of the costs is driven by clinical trials
- **Within clinical trials the costs of phase 3 trial logistics is the largest driver**
 - The solution lies in a leaner handling of large volumes and complexity of individual trials not in reducing the number of trials
 - Strategies like lean and JIT need to come into play

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Business case

External analysis 5/8

Business Case

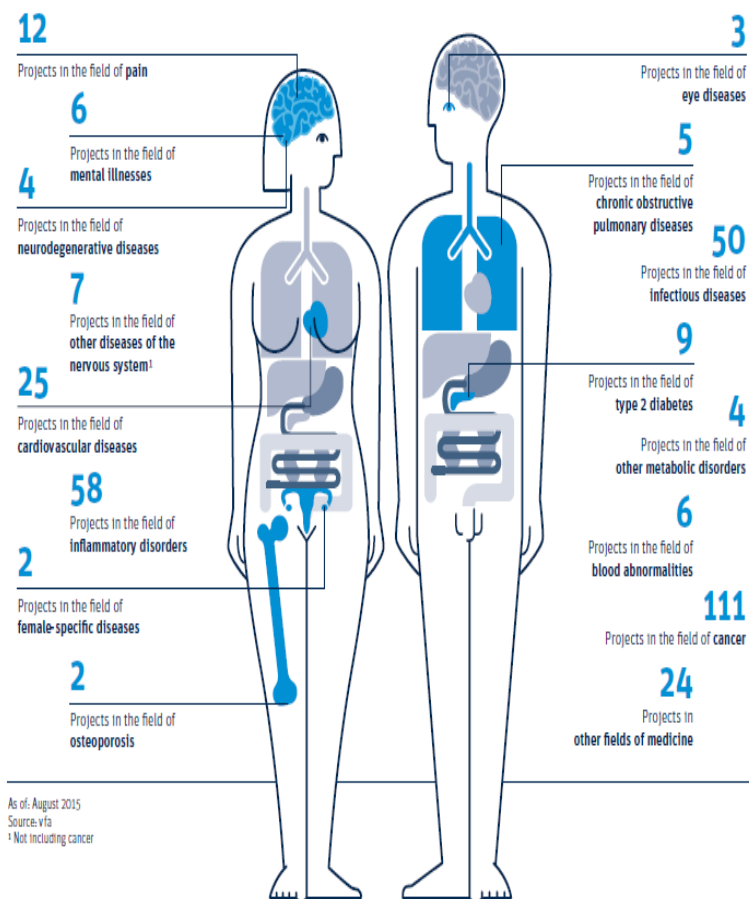
In a nutshell

Key concepts

Inner & Outer labels

Pharmaceutical projects of vfa companies promising approval by 2019

Distribution in various medical fields; total number of projects: 328



As of: August 2015
Source: vfa
¹ Not including cancer

- **No more block busters but drugs with a smaller therapeutic bandwidth**
 - The amount of patients that pay for a pharmaceutical decreases based on the smaller therapeutic bandwidth
 - So the increased costs for equal or less amount of new pharmaceuticals need to be paid by a smaller amount of patients
 - This requires new price/cost strategies
- Strategy 1 is collaboration with other LS partners
- Strategy 2 is cost reduction
- Strategy 3 is price increase

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Business case

External analysis 6/8

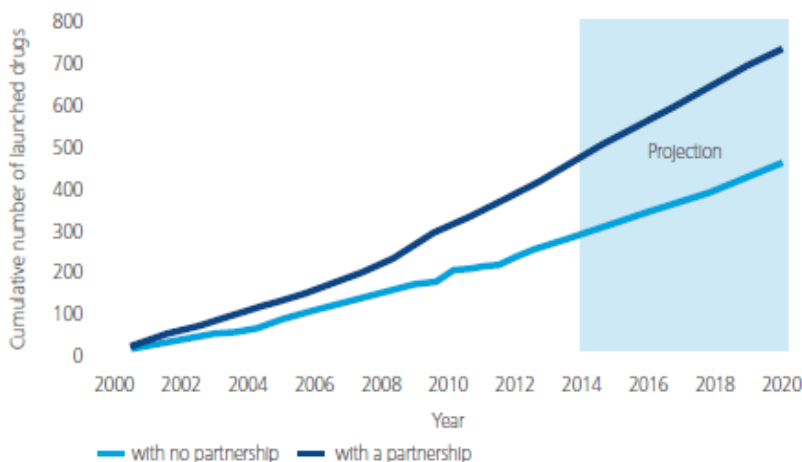
Business Case

In a nutshell

Key concepts

Inner & Outer labels

Drug Partnership deals: US launched assets since 2000



Source: Informa Plc, Biomed tracker, accessed May 2014

- No more block busters but drugs with a smaller therapeutic bandwidth
- **Strategy 1**
is collaboration with other LS partners
 - Share the costs is one strategy but it also means share the revenue
 - Collaboration poses new challenges in data/system harmonization and company cultures which result in somewhat increased total cost
- Strategy 2
is cost reduction
- Strategy 3
is price increase

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Business case

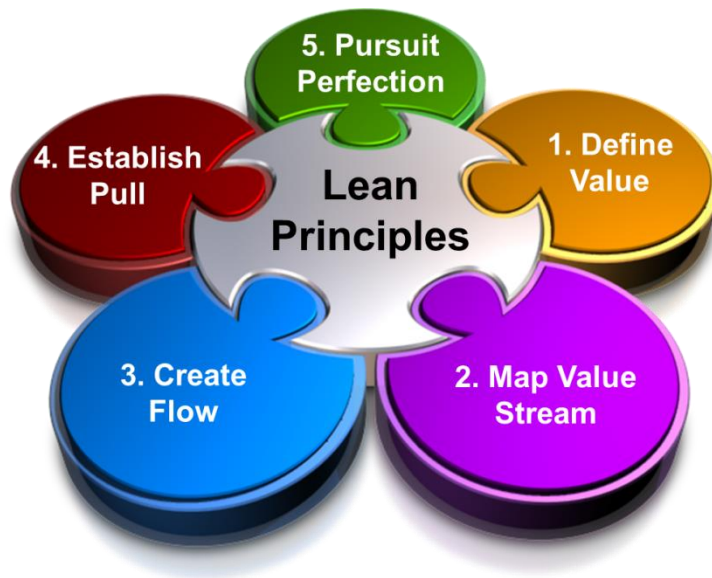
External analysis 7/8

Business Case

In a nutshell

Key concepts

Inner & Outer labels



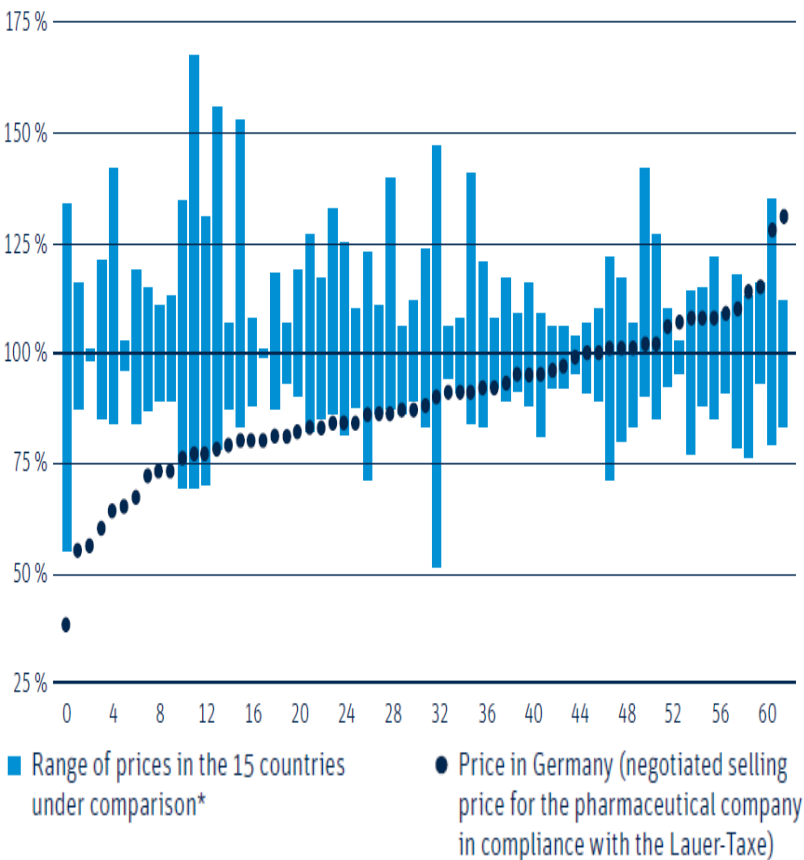
- No more block busters but drugs with a smaller therapeutic bandwidth
- Strategy 1 is collaboration with other LS partners
- **Strategy 2 is cost reduction**
 - Decreasing cost while maintaining or even improving on “volume and quality of result” is a craft that moved to the background but is now newly prioritized
 - It needs a culture and infrastructure of continuous process improvement
- Strategy 3 is price increase

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Business case

External analysis 8/8

Business Case	In a nutshell	Key concepts	Inner & Outer labels	
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- No more block busters but drugs with a smaller therapeutic bandwidth
- Strategy 1 is collaboration with other LS partners
- Strategy 2 is cost reduction
- **Strategy 3 is price increase**
 - The fast and easy solution
 - Stronger push back from authorities, getting to the question what is the value of a human live.....
 - High prices that seemed to be justified in biotech are now overtaken by much cheaper biosimilars

Source: ÖBIG, Lauer-Taxe (as of: May 2015)

* DNK, SWE, FIN, CZE, AUT, SVK, GRC, ITA, ESP, PRT, FRA, BEL, IRL, GBR, NLD

Business case

Internal analysis 1/1

Business Case	In a nutshell	Key concepts	Inner & Outer labels	
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- Lots of activities need to finish before the start of a packaging order, causing long lead times
- Expiry dates can be updated since stability testing is ongoing
- Patient enrollment is difficult to predict causing waste of material and activities
- 30% drug in patient is a not unusual yield
- The regulatory required label information is often a constraint although value add is ambiguous
- Earnings model for CMO's (per shelf, per order) are not an incentive for supply chain improvements

A difficult balance between demand uncertainty and supply complexity

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Business case

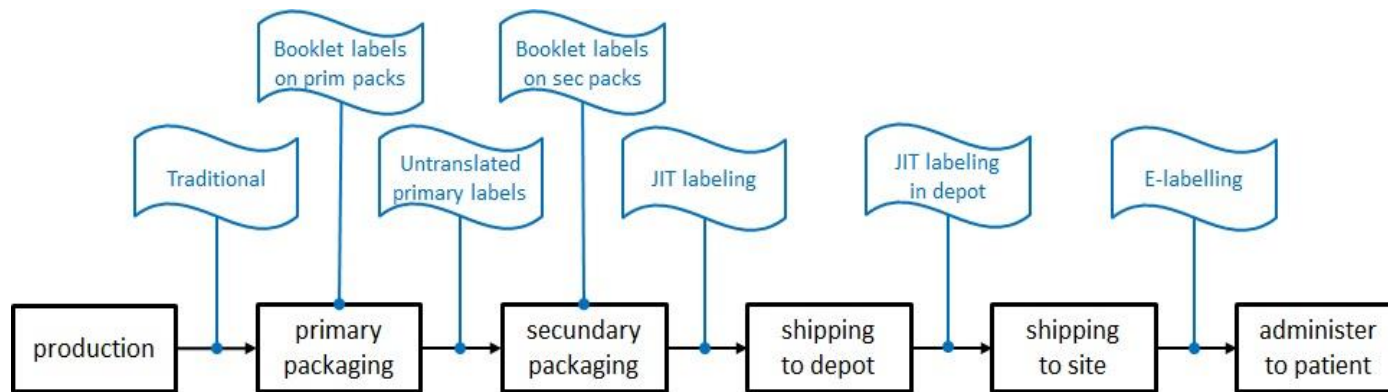
JIT Strategy 1/1

Business Case

In a nutshell

Key concepts

Inner & Outer labels



- Moving the decoupling point to the right means later end customization means less waste and better delivery reliability.
- There is no one size fits all; companies need a moveable decoupling point



The cost to develop a new pharmaceutical is growing and revenue needs to come from a smaller patient population.

Therefore development costs need to decrease and the clinical supply chain forms an important factor in that.

JIT will make the clinical supply chain leaner!

In a nutshell

Business Case

In a nutshell

Key Concepts

Inner & Outer labels

Serialized Packaging

Depot labelling

In a nutshell

Serialized packaging

Business Case

In a nutshell

Key concepts

Inner & Outer labels



- 2D serial barcodes are printed on cartons/bottles or are procured preprinted
- The barcodes are read in-line during packaging; system records which barcode represents which bright stock batch
- In case of multilevel also expiry date & kit number are made known to the barcode

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In a nutshell

Depot labelling

Business Case

In a nutshell

Key concepts

Inner & Outer labels



- In the depot for each kit the right label is printed and inspected with a camera
- The JIT station reads the 2D barcode on the kit to determine the right label information
- Wrong printed labels are invalidated
- Print exceptions report is the basis for a quick QP release

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The current way:

Secondary packaging & labelling in one packaging order

The JIT way:

Secondary packaging in a packaging order,
Secondary labelling per shipment request.

Key Concepts



Business Case	In a nutshell	Key Concepts	Inner & Outer labels	
		Design		
		Planning		
		Ordering		
		Packaging		
		Distribution		

Key concepts

Design



Business Case

In a nutshell

Key concepts

Inner & Outer labels

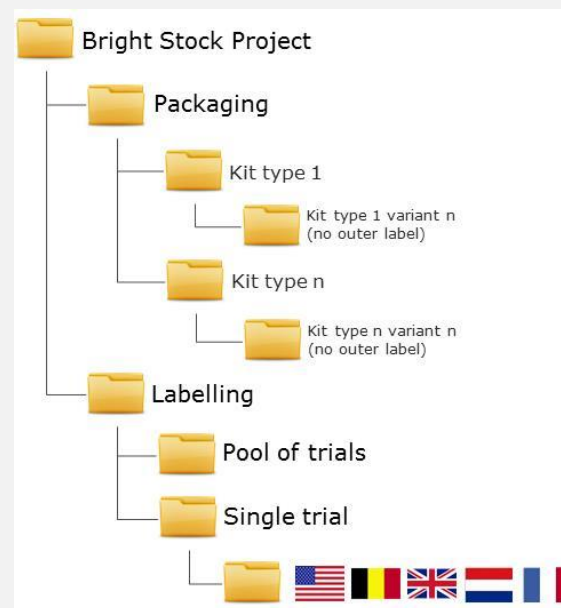
The current way

- Fixed monolithic design.



The JIT way

- Modular adaptable design.



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Key concepts

Planning



Business Case

In a nutshell

Key concepts

Inner & Outer labels

The current way

- Trial specific orders.

Study 1	Study 2	Study 3
Order 1 placebo	Order 2 placebo	Order 3 placebo
Order 1 active 1	Order 2 active 1	
	Order 2 comparator	
		Order 3 active 2

The JIT way

- Compound specific orders.

Study 1	Study 2	Study 3
Order 1 placebo		
Order 2 active 1		
	Order 3 comparator	
		Order 4 active 2

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Key concepts

Ordering



Business Case

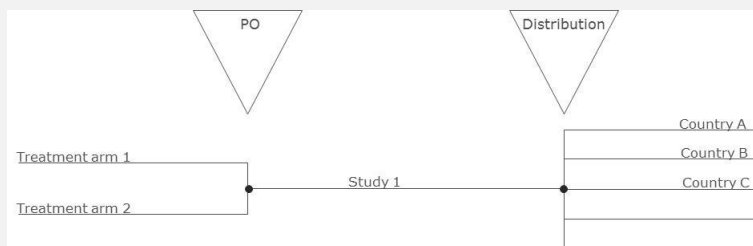
In a nutshell

Key concepts

Inner & Outer labels

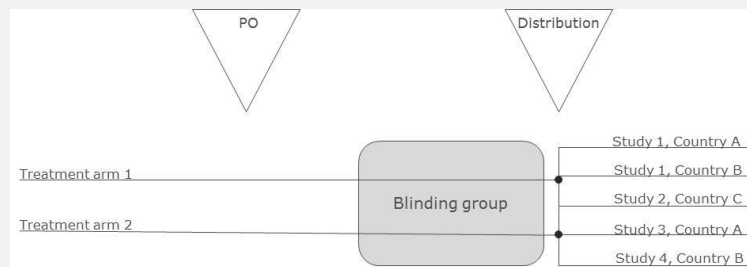
The current way

- Grouping of treatment arms before packaging
- Packaging orders trial specific
- Packaging orders country specific.



The JIT way

- Grouping of treatment arms after packaging
- Packaging orders not trial specific
- Packaging orders not country specific.



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Key concepts

Packaging



Business Case

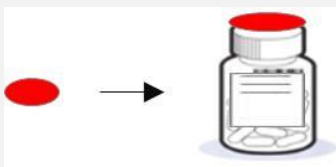
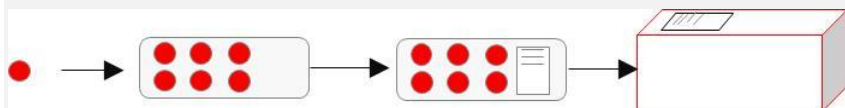
In a nutshell

Key concepts

Inner & Outer labels

The current way

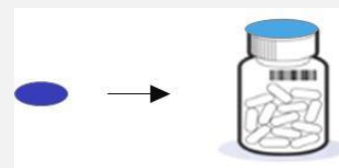
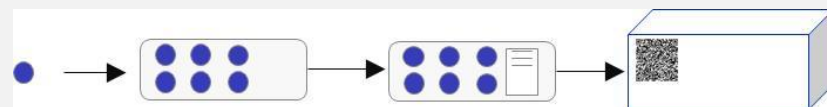
- Kits are secondary labelled.



- QP release for allowing shipments out of the packaging plant

The JIT way

- Kits are barcode serialized



- QA release for allowing batch allocation to a shipment order.

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Key concepts

Distribution



Business Case

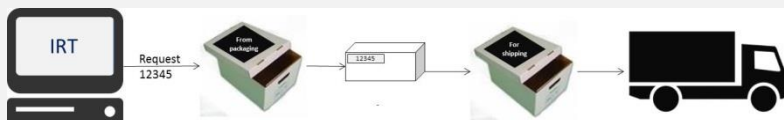
In a nutshell

Key concepts

Inner & Outer labels

The current way

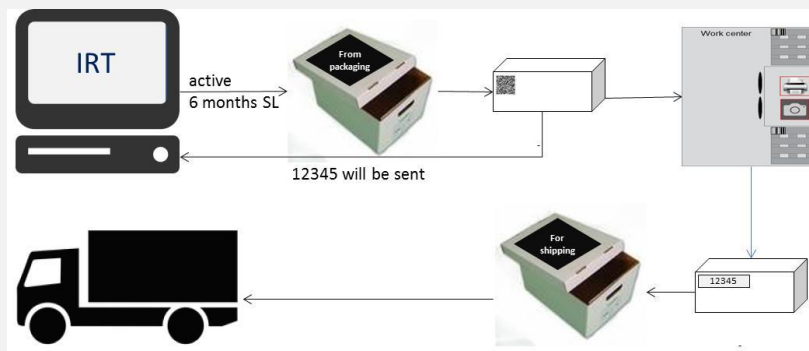
- Picking of kit numbers requested by IRT
- Kits are already labeled



- Kits are already QP released.

The JIT way

- Picking of kit type requested by IRT, IRT will be notified of picked numbers
- Kits are labeled per shipment order in depot



- Kits are already QA released and are QP released based on camera inspection of the labeling order.

Circuition



Implementing JIT is a change
of all elements of the operating model.

Technology enablement is key!

but also motivating the organization to go the extra mile!
and exceeding the benefits of a single department

Inner & Outer labels

Business case	In a nutshell	Key Concepts	Inner & Outer labels	
			Single level	
			Country independent	
			Multi-lingual labels	
			Booklet labels	

Inner & outer labels

Single level

Business Case		In a nutshell		Key concepts	Inner & Outer labels	
ref	Description	Untranslated inner label	Universal inner label	JIT outer label		
1a	Sponsor name	✓	✓	✓		
1b	Substance name	✓	✓	✓		
1c1	Dosage form	-	-	✓		
1c2	Route of admin	✓	✓	✓		
1c3	Dosage units	✓	-	✓		
1d1	Reference #	✓	-	✓		
1d2	Consignment #	-	-	✓		
1e	trial #	-	-	✓		
1f	Kit #	✓	-	✓		
1g	Investigator	-	-	-		
1h	Directions for use	-	-	-		
1i	For CT use only	-	-	-		
1j	Storage Conditions	-	-	✓		
1k	Expiry date	✓	-	✓		
1l	Keep out of reach....	-	-	-		

- No inner label by using single level packaging designs.
- One bright stock for all countries

Inner & outer labels

Country independent inner labels

Business Case		In a nutshell		Key concepts	Inner & Outer labels
ref	Description	Untranslated inner label	Universal inner label	JIT outer label	
1a	Sponsor name	✓	✓	✓	 1a) Sponsor name 1b) Substance name 1c2) Route of admin 1c3) Dosage units 1d1) Reference # 1f) Kit# 1k) Expiry date
1b	Substance name	✓	✓	✓	
1c1	Dosage form	-	-	✓	
1c2	Route of admin	✓	✓	✓	
1c3	Dosage units	✓	-	✓	
1d1	Reference #	✓	-	✓	
1d2	Consignment #	-	-	✓	
1e	trial #	-	-	✓	
1f	Kit #	✓	-	✓	
1g	Investigator	-	-	-	
1h	Directions for use	-	-	-	
1i	For CT use only	-	-	-	
1j	Storage Conditions	-	-	✓	
1k	Expiry date	✓	-	✓	
1l	Keep out of reach....	-	-	-	

- Now: Country, language and trial independent
- Soon: No Expiry date

Circuition

Inner & outer labels

Multi-lingual outer labels

Business Case		In a nutshell		Key concepts	Inner & Outer labels	
ref	Description	Untranslated inner label	Universal inner label	JIT outer label		
1a	Sponsor name	✓	✓	✓		
1b	Substance name	✓	✓	✓		
1c1	Dosage form	-	-	✓		
1c2	Route of admin	✓	✓	✓		
1c3	Dosage units	✓	-	✓		
1d1	Reference #	✓	-	✓		
1d2	Consignment #	-	-	✓		
1e	trial #	-	-	✓		
1f	Kit #	✓	-	✓		
1g	Investigator	-	-	-		
1h	Directions for use	-	-	-		
1i	For CT use only	-	-	-		
1j	Storage Conditions	-	-	✓		
1k	Expiry date	✓	-	✓		
1l	Keep out of reach....	-	-	-		

Multi-lingual label

English	Francais
1a) Sponsor name	1a) Nom du sponsor
1b) Substance name	1b) Nom de la substance
1c1) Dosage form	1c1) Forme posologique
1c2) Route of admin	1c2) Voie d'administration
1c3) Dosage units	1c3) Les unités posologiques
1d1) Reference #	1d1) Numéro de référence
1d2) Consignment #	1d2) numéro de lot
1e) trial #	1e) Numéro d'essai
1f) Kit#	1f) numéro de kit
1j) Storage Conditions	1j) conditions de stockage
1k) Expiry date	1k) Date d'expiration

Stacked label

Francais
English
1a) Sponsor name
1b) Substance name
1c1) Dosage form
1c2) Route of admin
1c3) Dosage units
1d1) Reference #
1d2) Consignment #
1e) trial #
1f) Kit #
1j) Storage Conditions
1k) Expiry date

- JIT outer labels for multilingual countries

Inner & outer labels

Booklet labels

Business Case		In a nutshell		Key concepts	Inner & Outer labels
ref	Description	Untranslated inner label	Universal inner label	JIT outer label	
1a	Sponsor name	☑	☑	☑	
1b	Substance name	☑	☑	☑	
1c1	Dosage form	-	-	☑	
1c2	Route of admin	☑	☑	☑	
1c3	Dosage units	☑	-	☑	
1d1	Reference #	☑	-	☑	
1d2	Consignment #	-	-	☑	
1e	trial #	-	-	☑	
1f	Kit #	☑	-	☑	
1g	Investigator	-	-	-	
1h	Directions for use	-	-	-	
1i	For CT use only	-	-	-	
1j	Storage Conditions	-	-	☑	
1k	Expiry date	☑	-	☑	
1l	Keep out of reach....	-	-	-	



- For shipments to regional depots, booklet labels will remain in place



For decades label requirements of which nobody recognizes the benefit dictated an inefficient and expensive way of working. With JIT the interpretations of these regulations are stretched, and the collaborative industry starts challenging the current regulations at all!

Circuition would be happy to help you innovate your Clinical supply chain

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 primary contact partner	:	Hans Heesakkers E: hans.heesakkers@circuition.org M: +31 654 642 648