

Stock-taking Conference on Applications for Authorisation

Expanscience/EDC case

**Iann Rancé – *Ph.D*, R&D Expanscience
November 13, 2017**

20 min talk - Plan

- **Expanscience & EDC (Annex XIV).**
- **Dossier for EDC extended use authorization**
- **(Continuous) Improvement of EDC confinement**
- **Solvent Substitution process at Expanscience**

Expanscience & EDC

Laboratoires Expanscience

- Family owned mid size company. Pharmacy & Cosmetic
- 1950, staff 1050, m€ 275 TO (55 % outside France)
- 17 subsidiaries, selling products in 90 countries

- Main Products:



Skin care / babies + expectant mothers



Osteoarthritis of hip & knee / Elders

- Long term CSR policy:



SOURCING WITH RESPECT™



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Expanscience & EDC



EDC

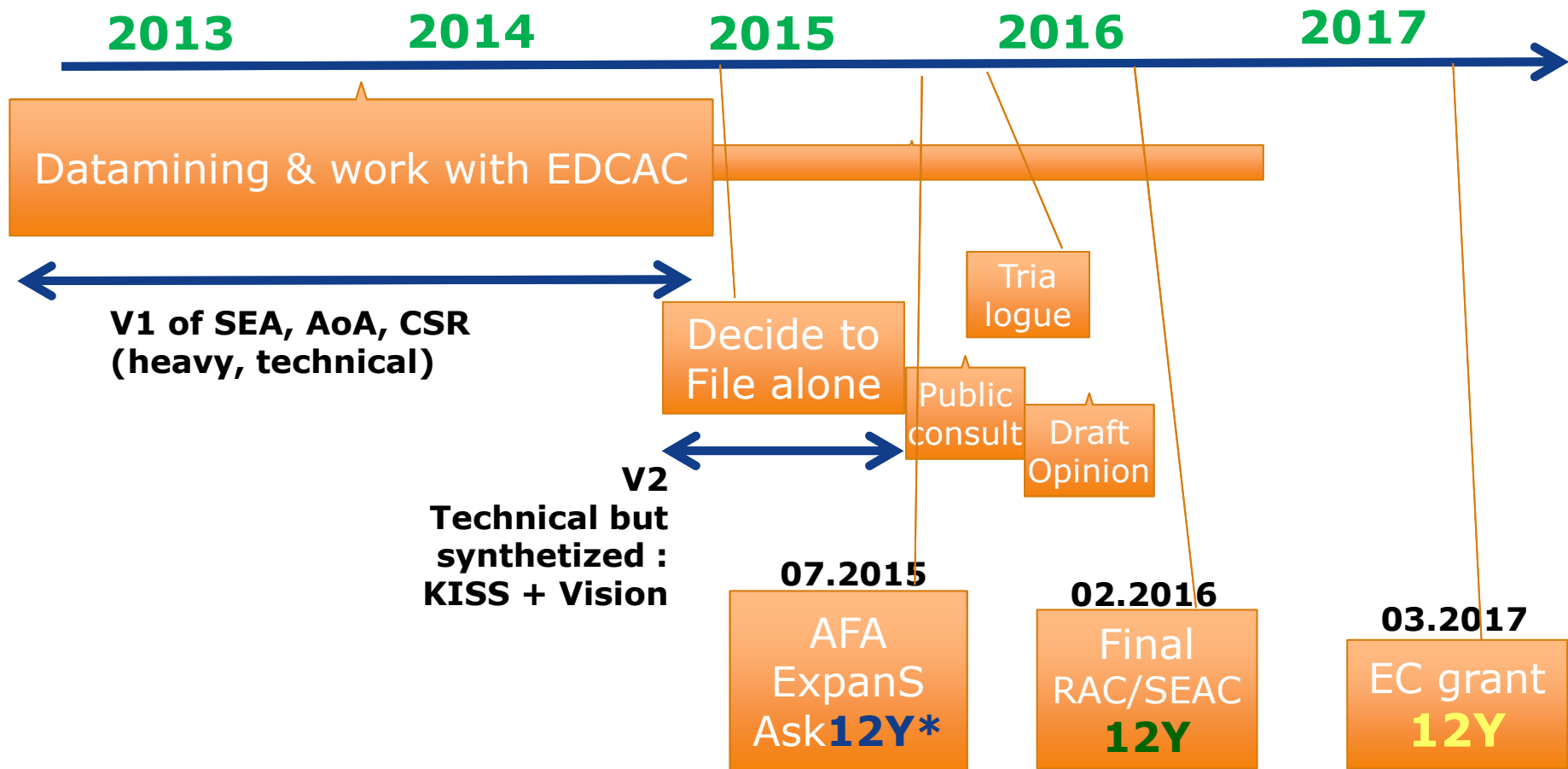
- High affinity solvent for our APIs (*active pharma Ingredients*)
- Used for 20+ years with constant and >99% recycling
- Last production step warrants < 15 ppb in final medicinal product

=Before inclus. Annex XIV
→ 100% internal company choice

- CMR. Start to work on EDC substitution in 2007
- EDC now listed to Annex XIV.
- Solvent needing autorisation for use after Nov 2017
- Expanscience applied for autorisation in 2015, work on dossier since 2014.
- Part of EDCAC with 10-12 other companies of Europe. But decided to file alone.

Dossier for extended use authorization of EDC

workflow



*** 12Y realistic but stringent**

Dossier for extended use authorization of EDC

+ & - of evaluation & filing

Plus / Benefit's

- Availability of unique contact, and commissions upon request
- Constructive & helpful commissions of experts
- Process is complex but clear
- Reach IT platform (not easy but all is there)

Minus / Concern's

- Delay for EC confirmation (13 Months): impacts substitution workflow & Investment.
- Rules change during process: Extention limit (12/15 to 20 y)
- UCLID versions changes, additional ressources

(continuous) improvement of EDC confinement

Equipment design improvements (change old ones)



=Before inclus. Annex XIV
→ 100% internal
company choice

23m€ - HQE Building



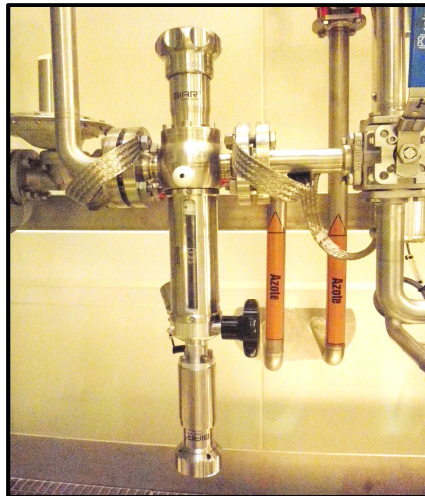
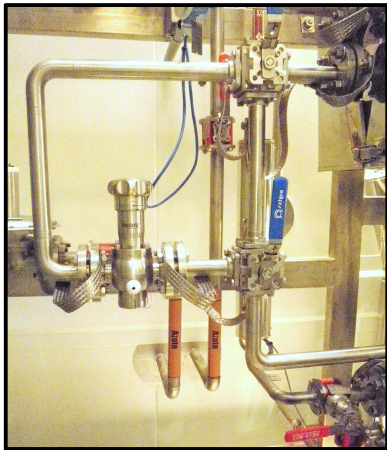
(continuous) improvement of EDC confinement

Equipment based-improvements (sampling valves)

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Leakproof & airtight



5 k€

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(continuous) improvement of EDC confinement

Education based-improvements (training... Training... Training...)

- Work practices need to be revised and explained:
- Training program in place : annual & on demand
 - New workers : training on hire (usually easy)
 - Experienced « old » workers (usually more difficult)
(I have done this way for decades & I know about it!)
- Assessment of Workers exposition in real life working conditions
 - Static sampling 8h at work post.
 - Dynamic sampling 8h on worker
 - Spotted at risk event : short sampling 15 min on worker

(continuous) improvement of EDC confinement

- 3 mesures statiques 8h côté colonnes de lavage :
 - Valeur moyenne : 1,31 mg/m³ < 83 mg/m³
 - Probabilité de dépassement VME : <0,1%
- 3 mesures statiques 8h côté flot tombant :
 - Valeur moyenne : 0,78 mg/m³ < 83 mg/m³
 - Probabilité de dépassement VME : <0,1%
- 3 mesures dynamiques sur un poste de travail - 8h (conducteur d'équipement) :
 - Valeur moyenne : 1,74 mg/m³ < 83 mg/m³
 - Probabilité de dépassement VME : <0,1%
- 2 mesures ponctuelles (15 min) sur prélèvements colonne de lavage :
 - Valeur moyenne : 4 mg/m³ < 208 mg/m³
 - Probabilité de dépassement VLE : <0,1%
- 1 mesure ponctuelle (15 min) sur conditionnement PIA + MIBK sortie Flot tombant :
 - Valeur : 9,54 mg/m³ < 208 mg/m³
 - Valeur < 10%VLE : probabilité de dépassement faible

Slides presented to workers during specific information sessions

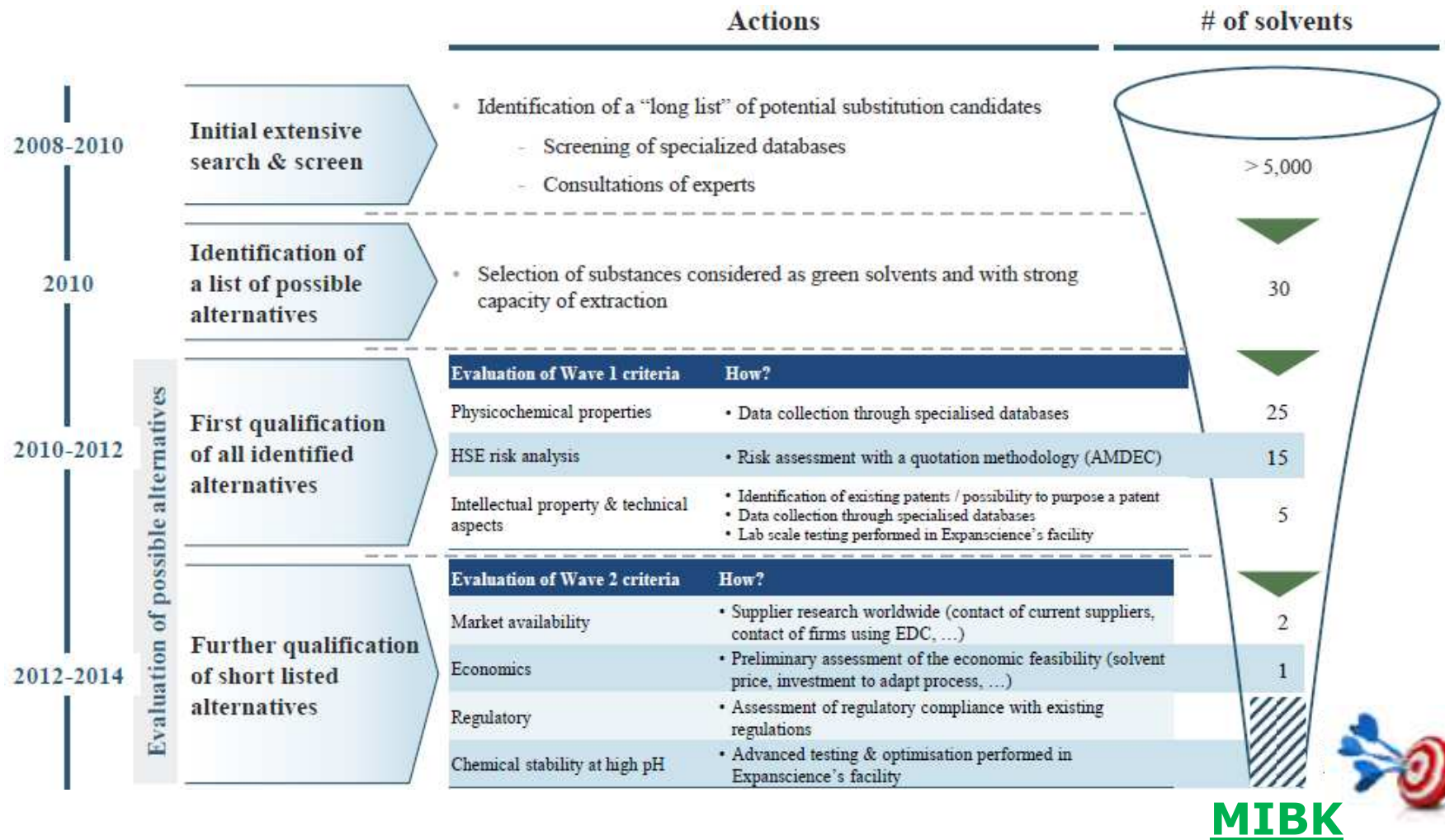
✓ Résultats conformes

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Substitution program

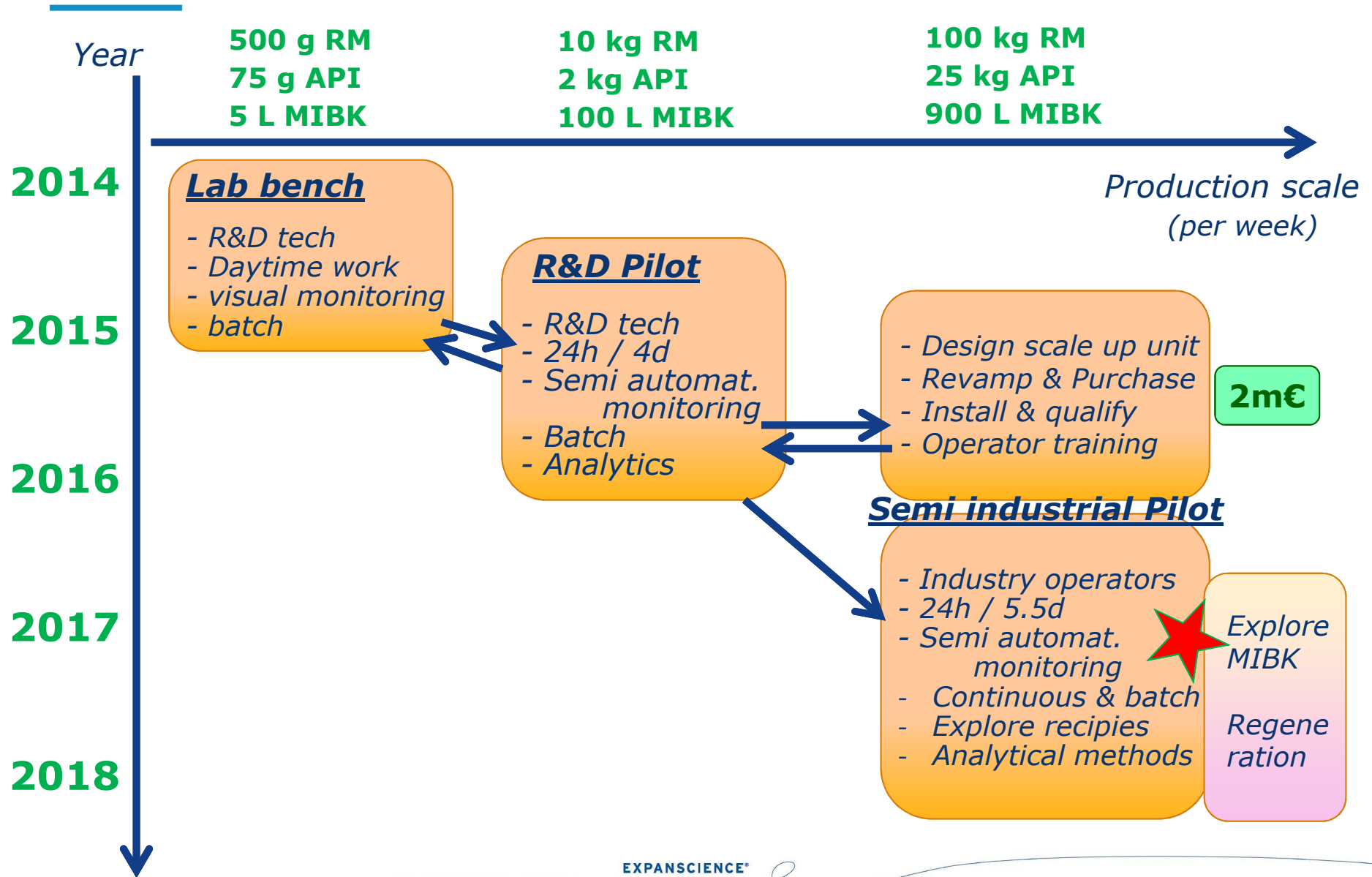
In pharma : a (very) long term story...



MIBK



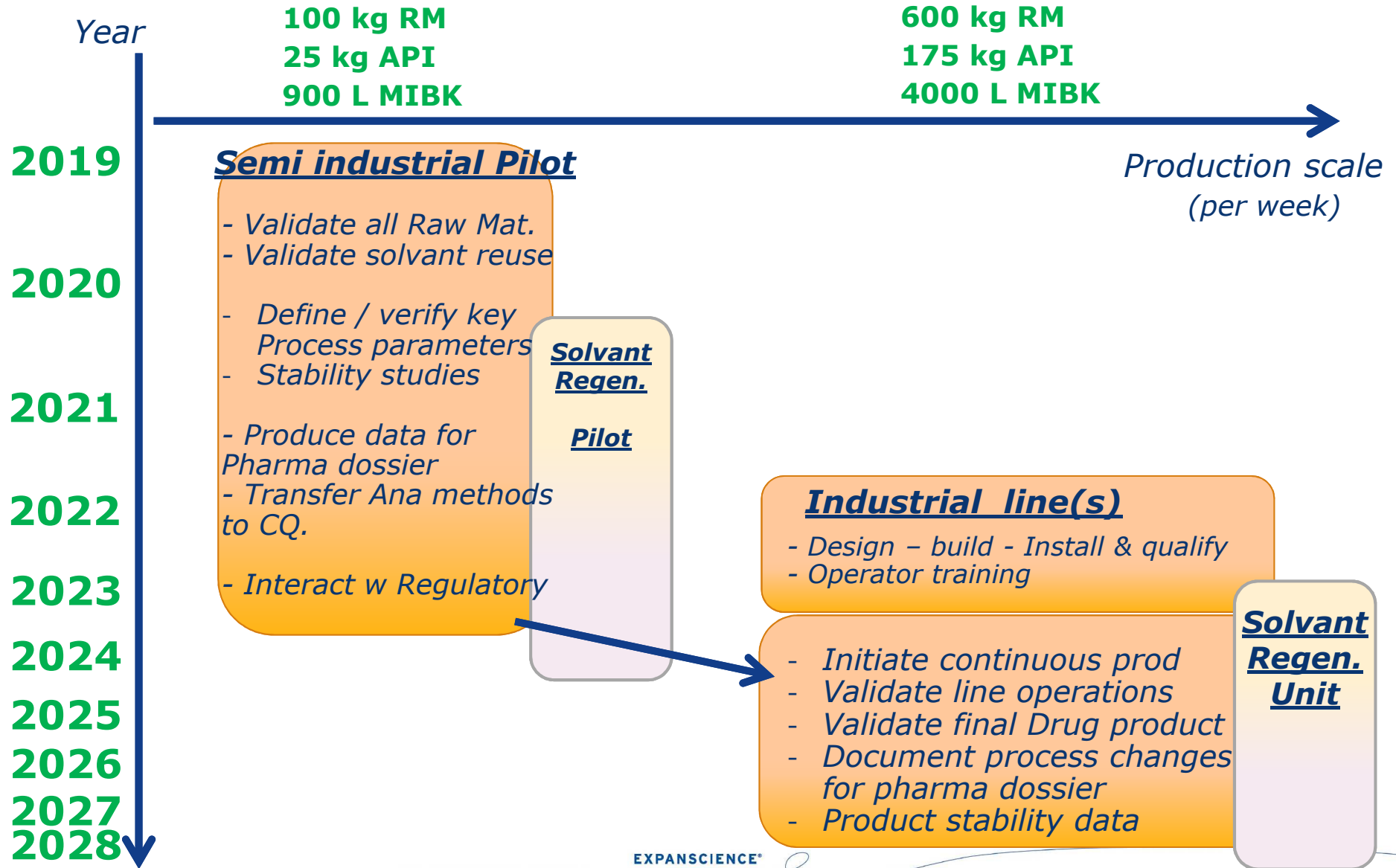
Substitution Program : where we are !



Substitution Program :

where we plan to be !

Non binding !!



EDC to MIBK...

Give FEEDBACK to EChA !!

Thanks to the audience

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***Iann Rancé / Caroline Baudouin
Laboratoires Expanscience
Innovation Research & Development
Rue des 4 filles, CS 20011
F-28233 Epernon Cedex - FRANCE***