PREMIÈRE MINISTRE
Liberté
Égalité
Fraternité

AGENCE DE L'INNOVATION EN SANTÉ

Secrétariat général pour l'investissement

French initiatives to promote novel methodologies of clinical research

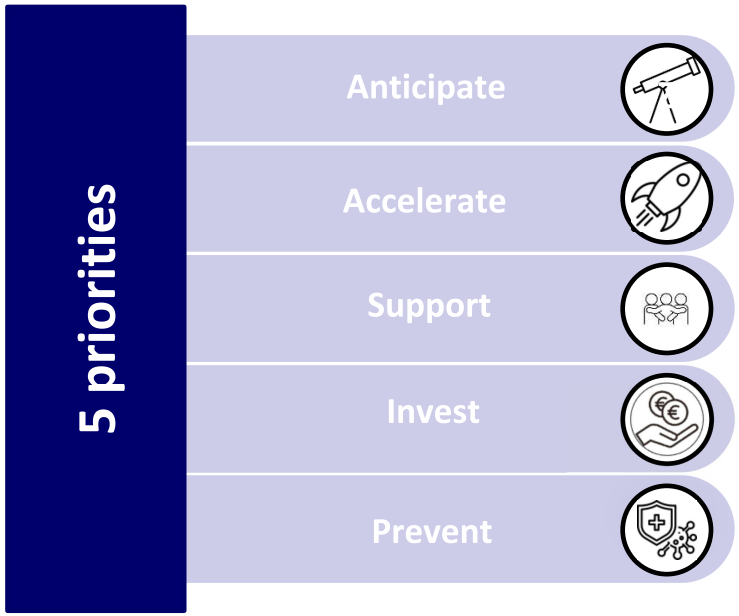
Clémentine BODY

French Health Innovation Agency

Health Innovation Agency - AIS

Under the authority of the **Prime Minister, its role is to coordinate** inter-ministerial work on innovation in healthcare

Created to manage the overall investment plan dedicated to health, with 7,5 billion euros of investment



Rely on the existing organizations and expertise

Working Party

F.CRIN FRENCH CLINICAL RESEARCH INFRASTRUCTURE NETWORK

FRANCE 2030 AGENCE DE L'INNOVATION EN SANTÉ

GOAL

Analyze and demonstrate concretely, thanks to a panel of use-cases, the benefit and added value of these approaches for speeding up the development/assessment of health innovations

What is new ?
- Hearing
- Analysis of Scientific Litt

What is accepted ?
- HAS assessments
- Opinions
- Concept papers and guidelines

Recommendations
- Scientific litt
- Partnership
- Methods / study using the methods

Use Cases

Call for project

1 What is new ? | 2 What is accepted ? | 3 Recommendations | 4 Use case

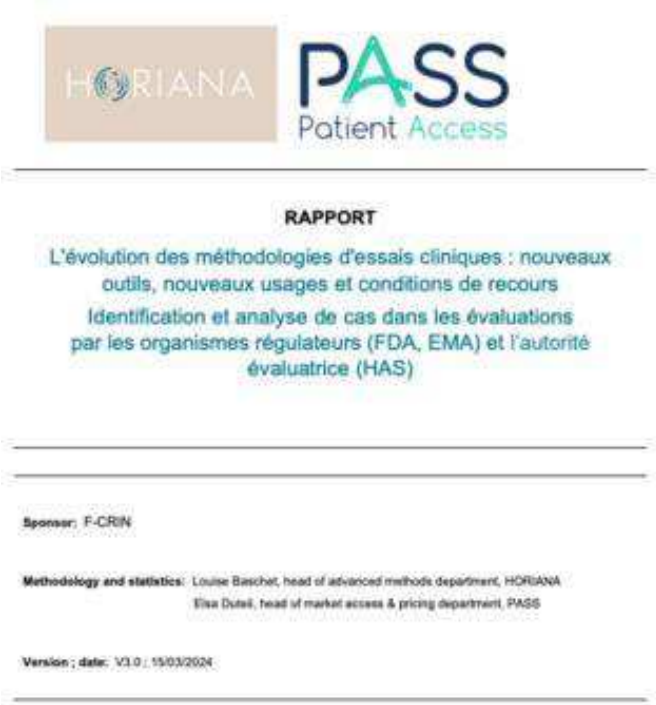




Adaptative enrichment	Plateform trial	External control	Bayesian trial	in silico trial
Sample size reassessment	Baskets trial		Pragmatic trial	Virtual partients with AI
Sequential Designs	Umbrella trial		Observational study	Stratification with AI
Seamless Designs			Enhanced trial	
MAMS				

Selected methodologies | Non selected methodologies

Analysis of Regulatory/HTA opinions for these new methodological approaches design


HORIANA PASS Patient Access

RAPPORT

L'évolution des méthodologies d'essais cliniques : nouveaux outils, nouveaux usages et conditions de recours

Identification et analyse de cas dans les évaluations par les organismes régulateurs (FDA, EMA) et l'autorité évaluatrice (HAS)

Sponsor: F-CRIN

Methodology and statistics: Louise Baschet, head of advanced methods department, HORIANA
Elsa Duteil, head of market access & pricing department, PASS

Version ; date: V3.0 ; 15/03/2024

600 opinions including novel methodologies among 11 280 issued by HAS

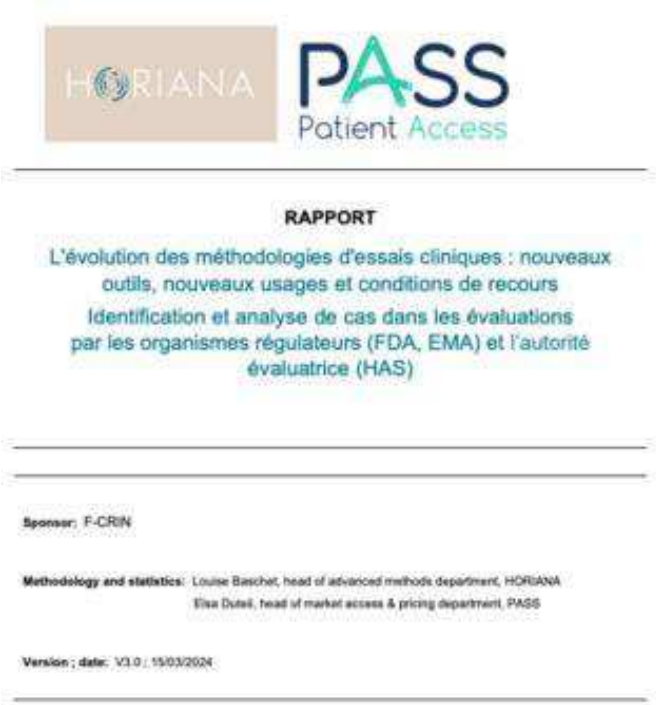
→ Novel methodologies **rarely used for market access purpose** (only in specific circumstances: COVID, rare diseases)

- Seamless Designs (When Ph2-3),
- Platform trial (1 Covid),
- Bayesian trial

- Basket trial
- Single arm trial

- Simulation
- Pragmatic
- IA tools
- Augmented trial

Analysis of Regulatory/HTA opinions for these new methodological approaches design


HORIANA PASS Patient Access

RAPPORT

L'évolution des méthodologies d'essais cliniques : nouveaux outils, nouveaux usages et conditions de recours

Identification et analyse de cas dans les évaluations par les organismes régulateurs (FDA, EMA) et l'autorité évaluatrice (HAS)

Sponsor: F-CRIN

Methodology and statistics: Louise Baschet, head of advanced methods department, HORIANA
Elsa Duteil, head of market access & pricing department, PASS

Version ; date: V3.0 ; 15/03/2024

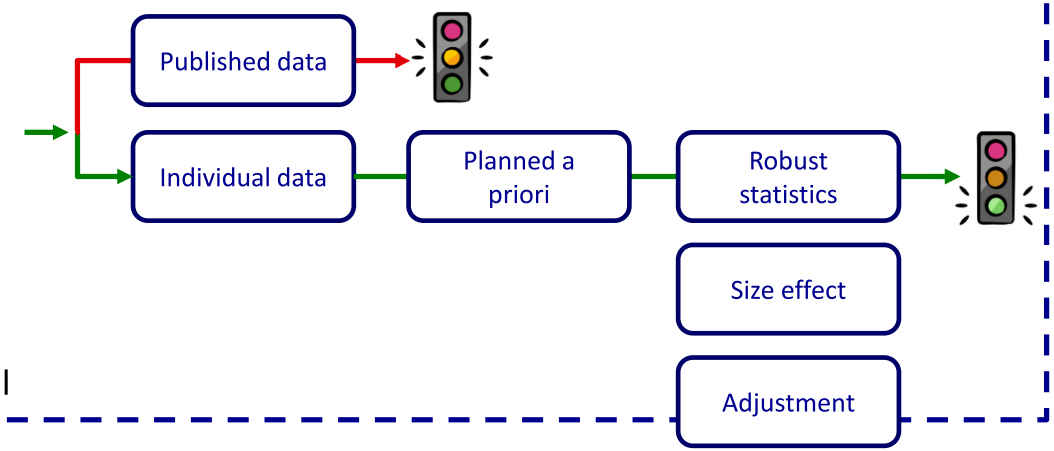
600 opinions including novel methodologies among 11 280 issued by HAS

→ Novel methodologies **rarely used for market access purpose** (only in specific circumstances: COVID, rare diseases)

- Seamless Designs (When Ph2-3),
- Platform trial (1 Covid),
- Bayesian trial

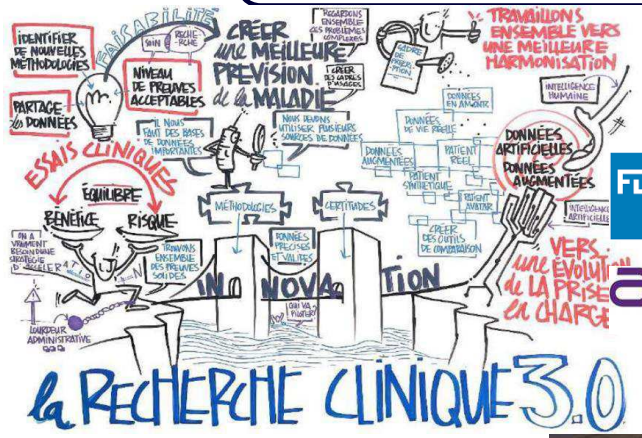
- Basket trial
- Single arm trial

- Simulation
- Pragmatic
- IA tools
- Augmented trial



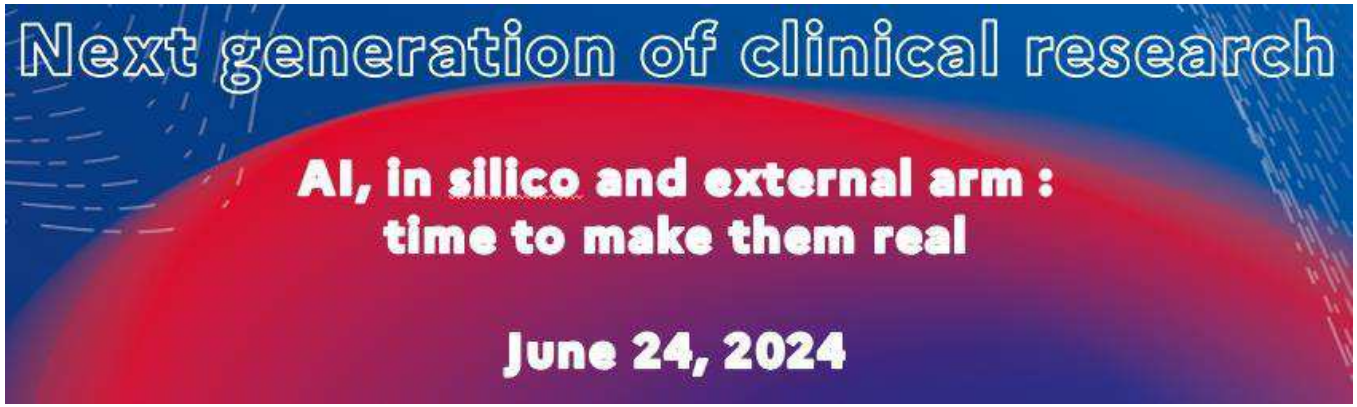
3 reports , 2 dedicated to the use of data (real world or artificial)

International Event dedicated to novel methodologies (Lille, June 2024)



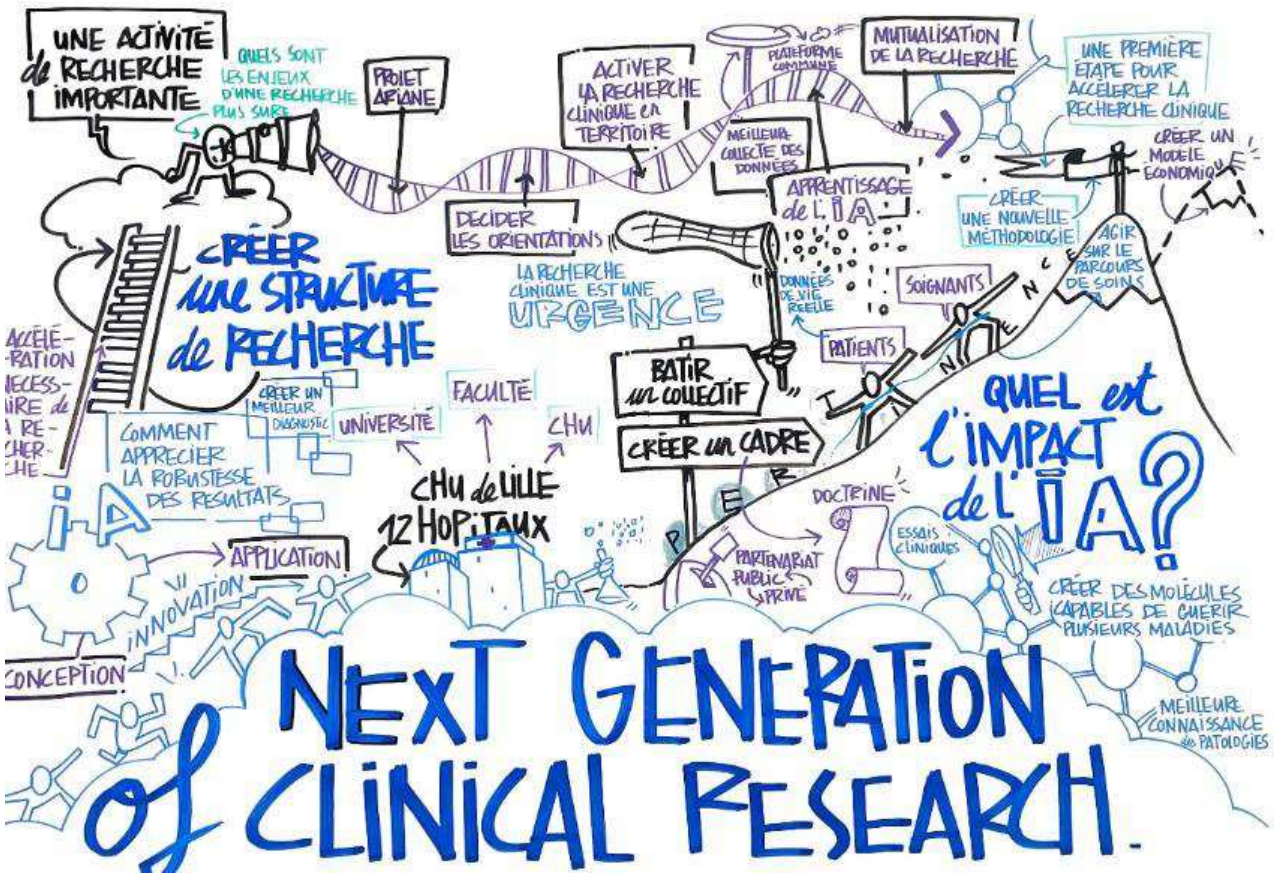
Evolution of the French legislation

Example : to facilitate the use of real world data in a clinical research (consent, information..)



- → Back to the needs
- → External / Hybrid arms
- → Slowly progressing diseases
- → For an ambitious regulation
- → Is there a pilot in the rocket ?

- → AI, diagnosis, prediction, organization of care
- → Digital Medical device
- → Emulated or simulated
- → AI to increase and optimize
- → Time to move on

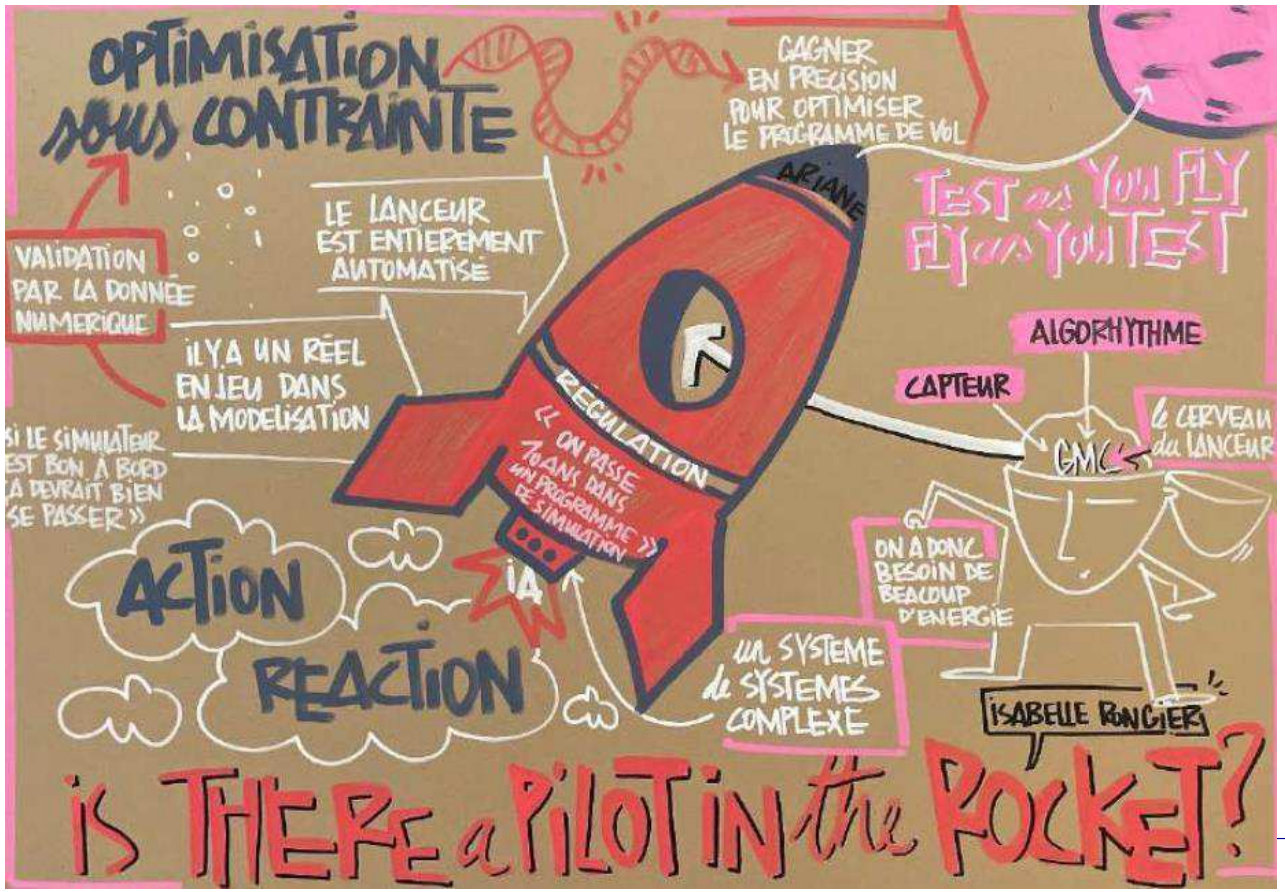


Back to the needs

Opportunities to improve clinical research, for the benefit of patients thanks to :

- ✓ Multidisciplinary collaboration
- ✓ Integration of new technologies

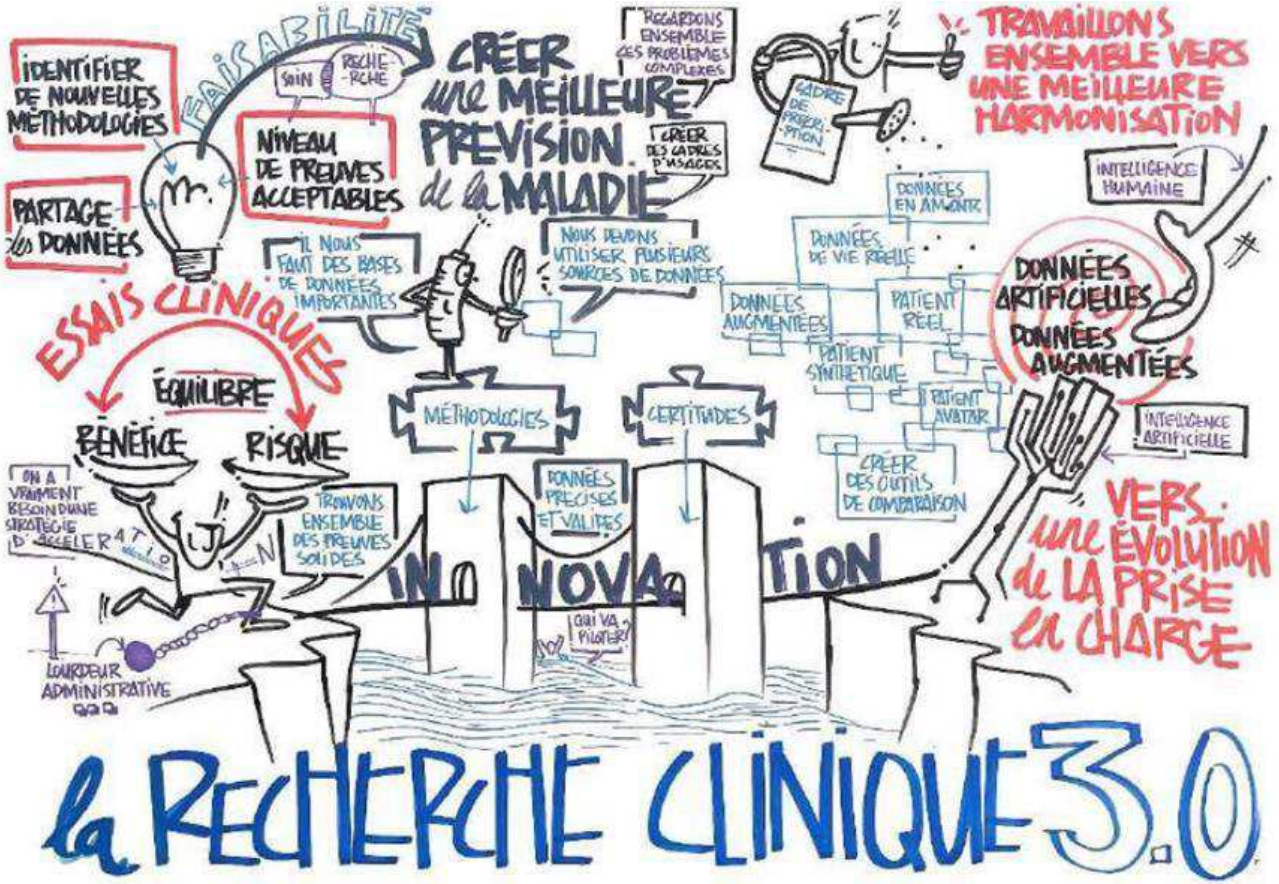
→ Need to focus on patient needs !



Is there a pilot ?

Introducing …. Ariane Group

→ Need for simulation when numerous complex systems are involved, to guarantee safety of astronauts !



External control arms
Slowly progressing diseases

3 pillars to simulate slowly progressing diseases :

→ Disease models
→ Treatment models
→ Analysis on virtual population

External control arms when RCTs are difficult :

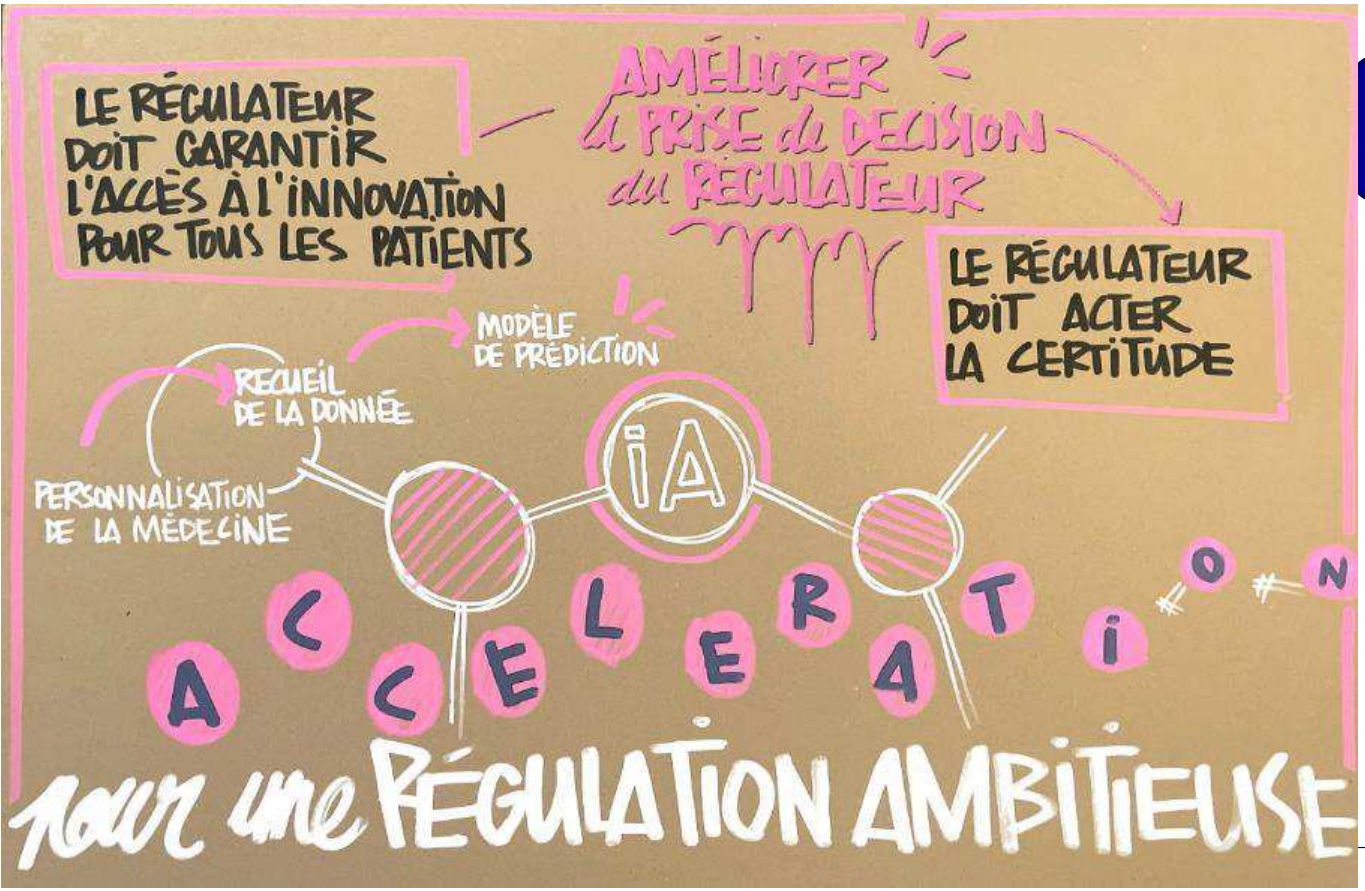
- Rare diseases
- Long follow-up required

RWE are a good opportunity to address these challenges

Emulated or simulated ?

Concrete situations where emulated / simulated trials have an interrest :

- Difficulties to recruit in control arm
- Seeking for a conditionnal approval
- Need to compare to SOC



Keynotes

Lionel Collet – HAS President:

- Novel methodologies integrated since 2013 in Commission's doctrines
- Need for a balance between novel methodologies and robust data

Alexandre de la Volpilière – ANSM

- Data collection become a pivotal issue
- Need for European coordination

Digital Medical Devices

DMD may bring an improvement in terms of organization of care :

This impact on organization of care needs to be assessed by Authorities, which may define a clear assessment framework.

Assessment initiatives (sandboxes) at Eu level are key to deploy those devices

AI for clinical research

AI can predict the course of disease, and optimize recruitement.

Need for a close collaboration between industry, authorities and academics:

- **Communication**
- **Training and seizing**
- **Assessment and validation**

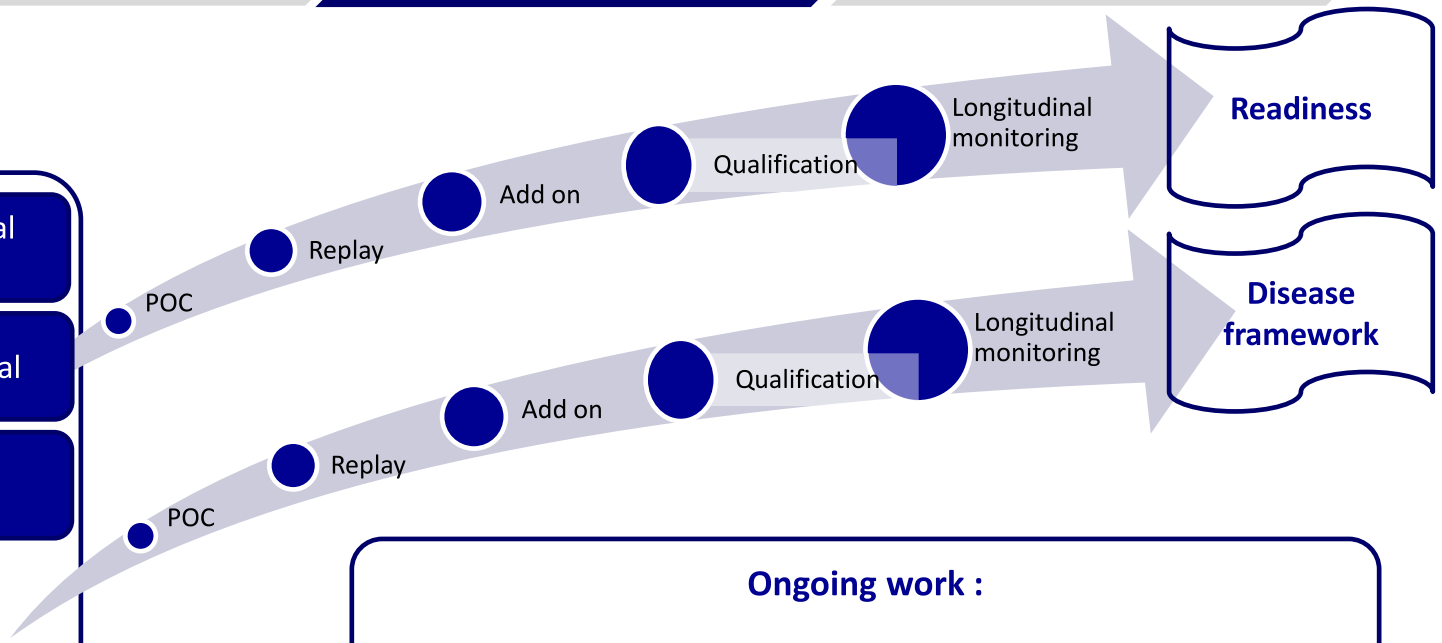
Time to move on

Next steps :

- Communication and transparency
- All stakeholders involved (patients, HCPs, general population)
- Collaboration between academics, industries, authorities, patients ..
- Clear regulatory framework
- Continuous improvement

1 What is new ? | 2 What is accepted ? | 3 Recommendations | 4 Use case

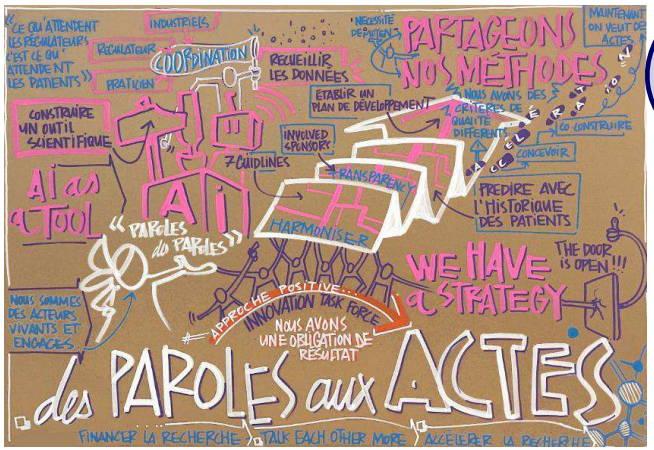
- Virtual patients
- Emulation / external control arms
- AI and pronostic adjustment
- Emulation target trial
- AI and predictive adjustment
- Enhanced arm
- In-silico model disease



Ongoing work :

⇒ Consider what is "**fit for purpose**" (in silico models, AI adjustment) and **methodological framework** (emulation, virtual patient, digital twin …)
⇒ Pathway for clinical validation (level of readiness)
⇒ Regulatory risk

1 What is new ? | 2 What is accepted ? | 3 Recommendations | 4 Use case



Call for project

Identify **clinical study projects** able to compare the value of these novel methodologies to the standard RCT in terms of:

- Performance (recruitment, duration, costs)
- Level of proof with similar security requirements

What is expected ?

- **Modeling and simulation:** virtual patients (in silico, AI)
- **Advanced tools:** machine learning/artificial intelligence, innovative methods for adjusting statistical models, validation of substitution criteria, etc.
- **Augmented arm** (or hybrid)
- **Real world arm / study :** emulation; enrichment of data sources (cohorts, registers, warehouses)

Benefit for selected projects

1. Identification and promotion of **success stories**
2. **Technical support** from WG experts
3. **Institutional support** (HDH, CNIL, ANSM…) throughout the project
4. **Financial support** (ex : ancillary studies to demonstrate and measure the value of using different methodological approaches)

PREMIÈRE
MINISTRE
Liberté
Égalité
Fraternité

Secrétariat général pour l'investissement