

Implementation of Bayesian thinking within Industry

FEEDBACKS FROM BIOMERIEUX

PIONEERING DIAGNOSTICS

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- **BioMérieux:** *world leader on IVD*

- **BioMathematics groups:**

Organization, Missions and skills

- **Bayesian thinking implementation**

 - *Why?*

 - *How?*

 - *Where are we today*

- **Discussion:** Success factors and challenges

BIOMERIEUX



A WORLD LEADER IN *IN VITRO* DIAGNOSTICS

MISSION

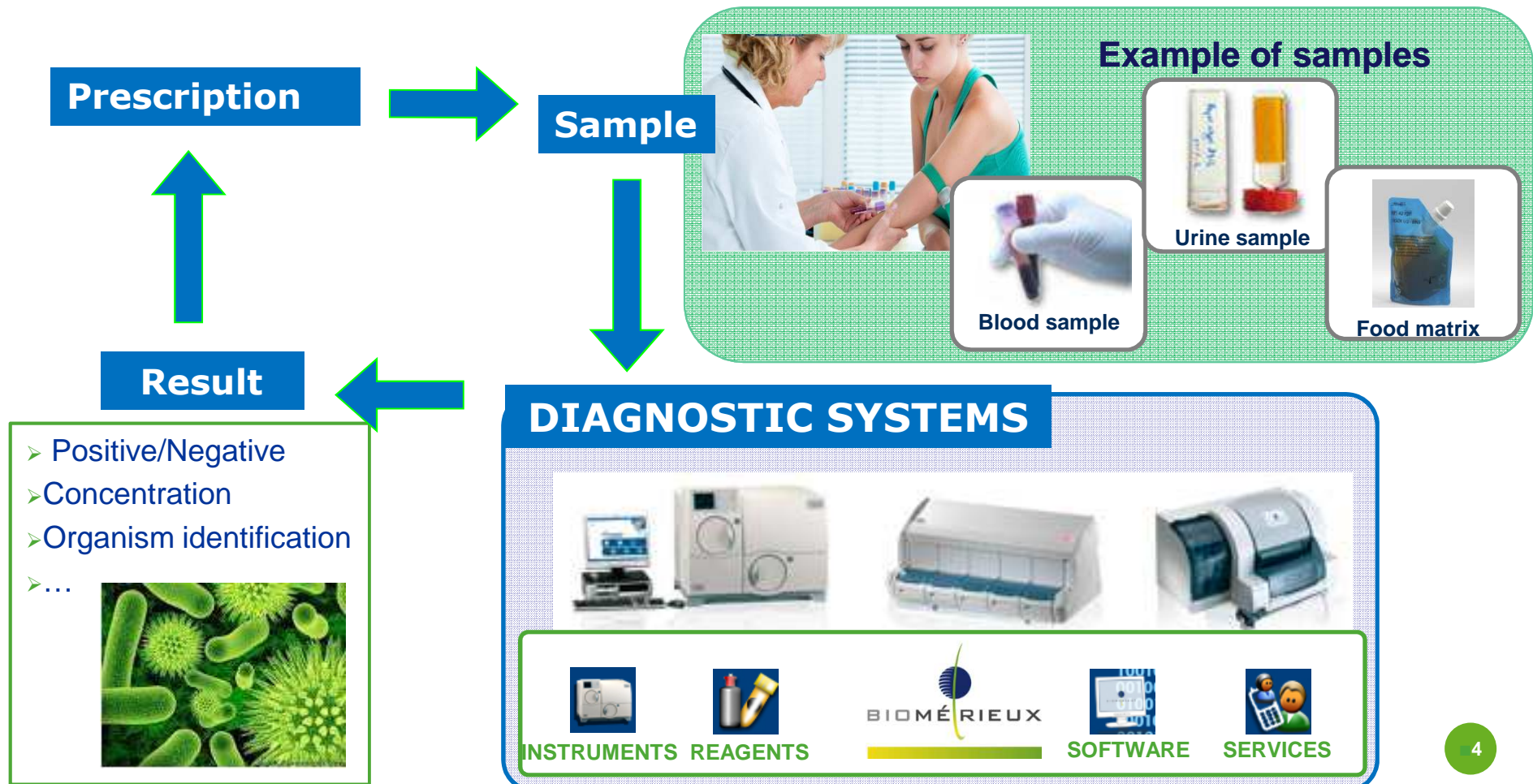
- Contribute to the improvement of public health worldwide through *in vitro* diagnostics



What are *In Vitro* Diagnostics?

- An *In Vitro* Diagnostic is a method of performing diagnostic test, outside of a living body, in an artificial environment.

IVD can be used to detect diseases, conditions, or infections.



BioMérieux: 2 fields of activities

■ The clinical field (~ 80% of sales):

Improving patient health

- A complete range of diagnostic solutions for the diagnosis of:
 - infectious diseases
 - cardiovascular diseases
 - targeted cancers



■ The industrial field (~ 20% of sales):

Ensuring consumer safety, product quality and animal health

- Solutions for detecting microorganisms in order to prevent and track product contamination in:
 - food
 - biopharmaceuticals and cosmetics
- A complete range of veterinary diagnostic solutions for:
 - infectious diseases
 - fertility monitoring



Product offering based on 3 key technologies of in vitro diagnosis

Immunoassays



Vidas



Microbiology

BLOOD CULTURE



VIRTUO™

PPM chromID®



Mass spectrometry
VITEK® MS



IDENTIFICATION
and/or ANTIBIOTIC
SUSCEPTIBILITY TESTING

PREVI® Isola



CULTURE

Molecular Biology



NucliSENS® easyMAG®



ARGENE

■ A large installed base of 79,500 instruments (as of December 31, 2014)

BIOMATHEMATICS GROUP

OUR MAIN MISSIONS

- Contribute to design fit for systems and reagents
- Guide their transition from design to production
- Help support product operation on the field
- Train the different functions across the product lifecycle

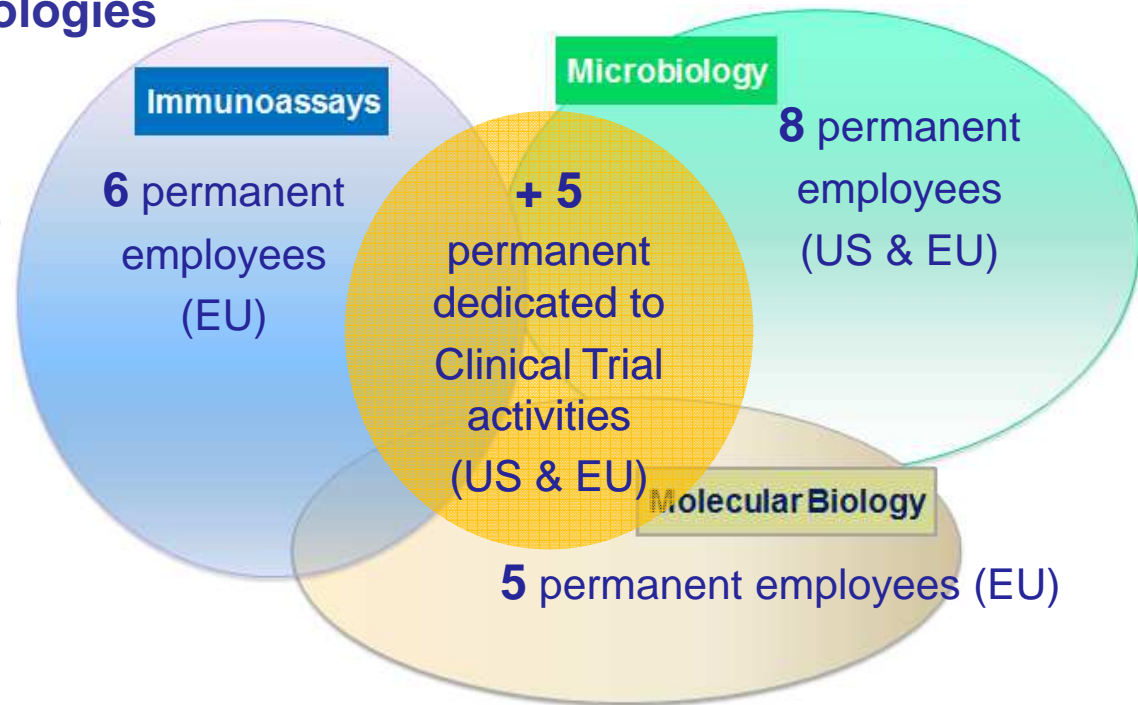
....and mitigate the risk of deadly sins...



Organization and skills

- Within R&D organization
- Related to the 3 key technologies

*Organization to better serve
our partners with skills
adapted to the technology*



- Main background:

Master degree (or equivalent) in statistics or applied mathematics

- ~ 50% of the team with dual training

Biology/Chemistry – Bioinformatics – Computer sciences, ...

Development steps:



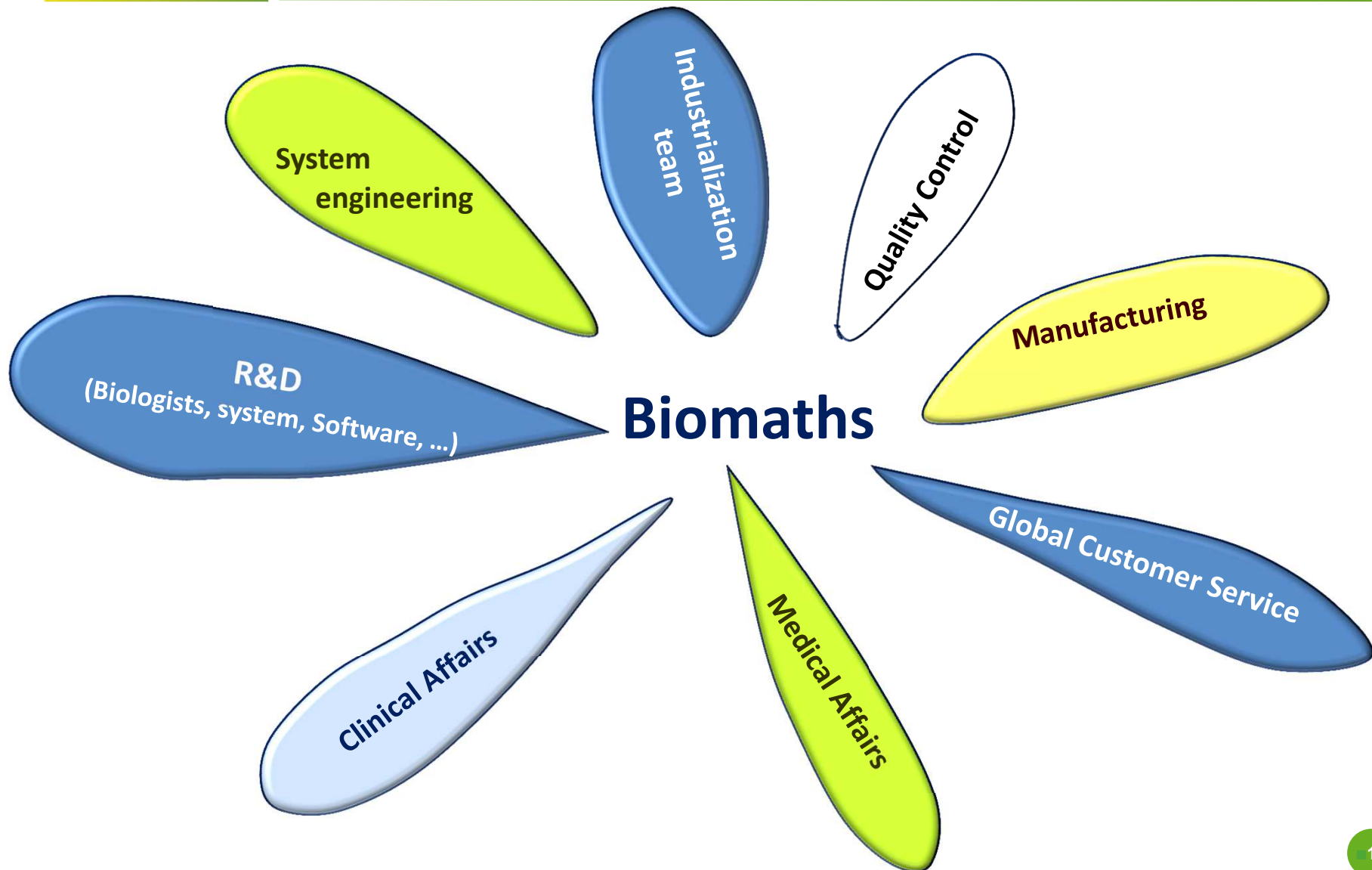
Methods

- Descriptive statistics
- Inferential statistics
- Machine Learning
- Mathematical modeling
- Design Of Experiments
- Sample size
- Control Charts
- Exploratory data analysis
- Uncertainty of measurement
- Bayesian statistics

cut-offs determination				
		Comparisons Trends	Accuracy profile for analytical methods	
ID Classifiers	Cross Validation			
Data reduction algorithm				
	Optimization Robustness			
		Clinical trials		
			Manufacturing trends/ SPC	External QC
Variables correlation				Complaints Investigations
	Metrological traceability			
			Specification setting	

*Biomaths activities:
Some examples*

Our internal partners: many different functions



Global Functional Excellence organization

■ The goal of functional excellence is to promote **collaboration** and share **best practices** to ensure **high-quality** and **customer-valued** deliverables

- **Collaboration:**

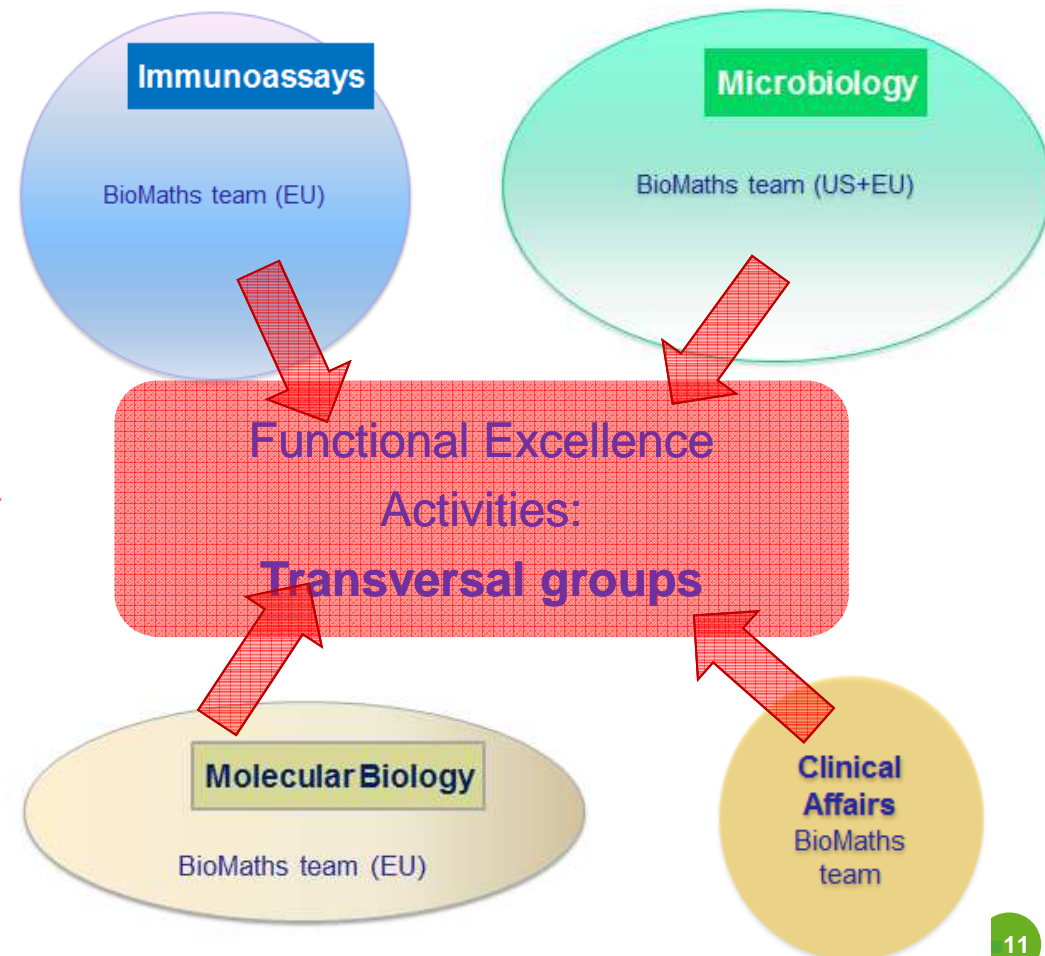
Connect and build communities of BM people working on similar topics

- **Best BM practices** in terms of methods, processes, tools

- **High-quality:** deliverables compliant to international standards & guidelines

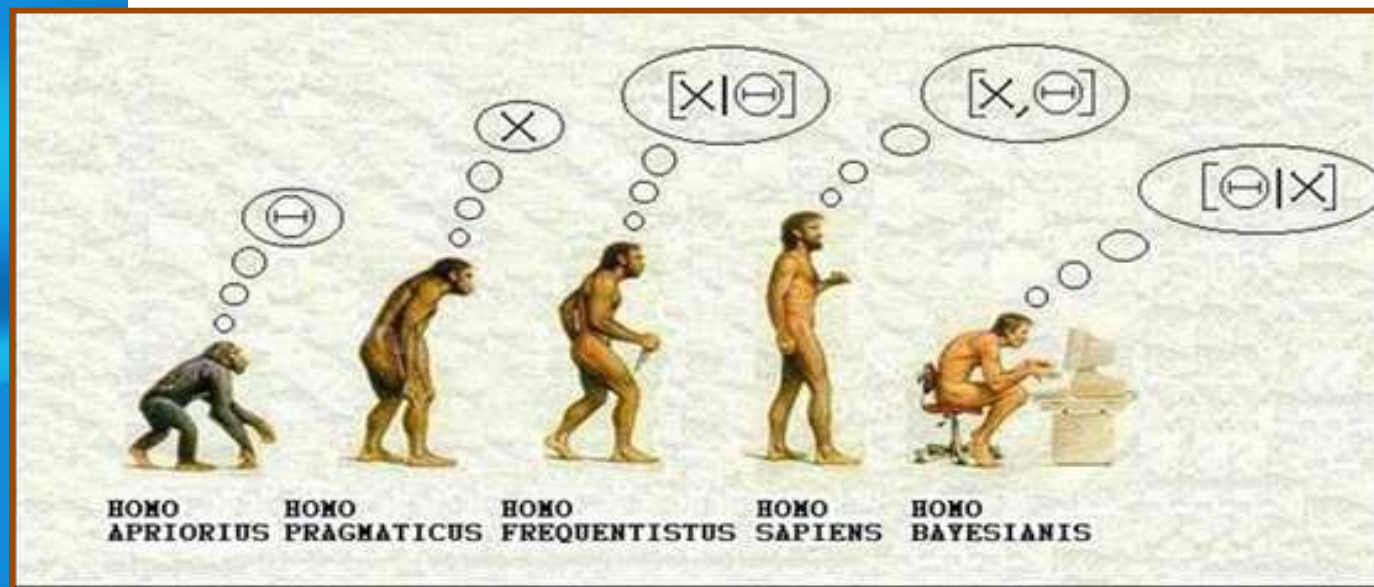
- **Customer valued:**

Ensure that the methods used are bringing the most value as possible to our internal partners/external customers



BAYESIAN STATISTICS **IMPLEMENTATION**

Development of Bayesian Statistics skill



Is Homo-Bayesianis the new BioMaths evolution stage?



Why Bayesian Statistics within BioMérieux?

BioMérieux
TRIGGER

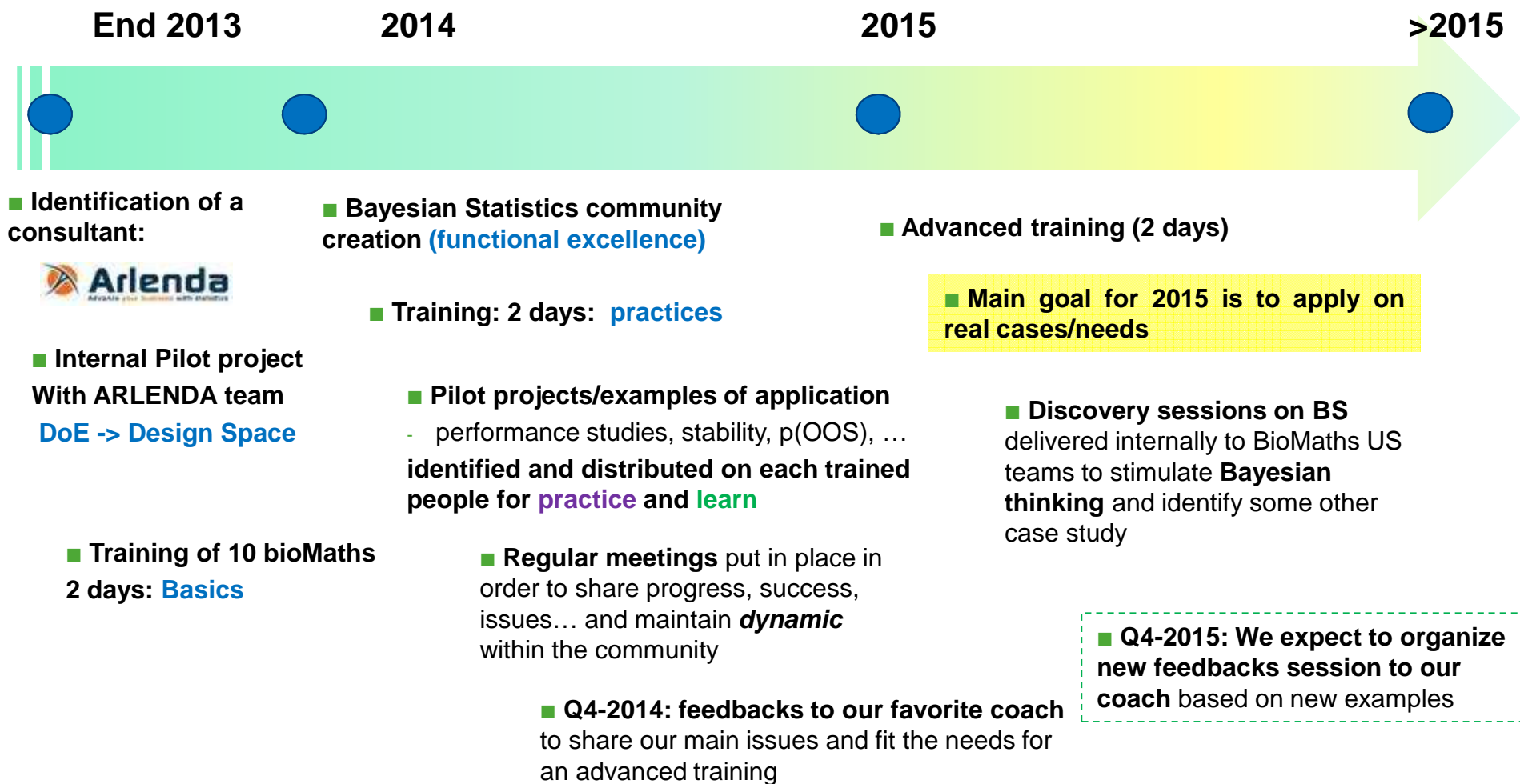
- To be prepared to the changing regulatory environment of the (bio)pharmaceutical world
(Quality By Design concept – ICH Q8-Q9-Q10)

Customer valued
deliverables
DRIVER

- **Allowing to incorporate prior information** (either expert opinion or historical knowledge) **into the analysis**
... and not only base our conclusions on one set (the last one) of experiments
- **Allowing to communicate findings in terms of probability notions that can be more easily understood by non-statisticians**
... instead of point estimate and “hypothesis that are/are not significantly rejected.”
- **Allowing to make predictions about the future behavior of methods/processes**



How Bayesian Statistics: Storyboard



2014: Collaboration with ARLEND on QBD project

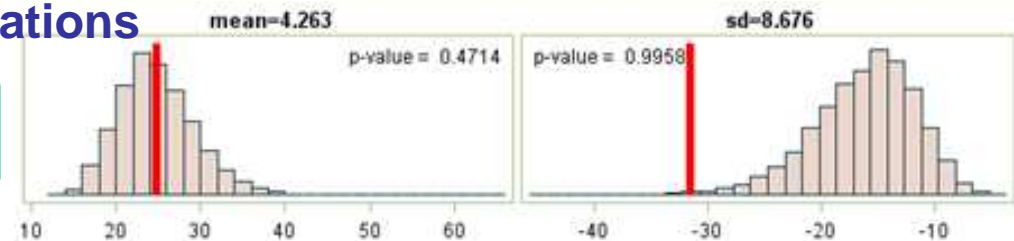
Design Space to be defined for a process with 10 Parameters & 6 Quality Attributes

Some of the pilot examples

Advantage

■ Probability to be Out Of Specifications

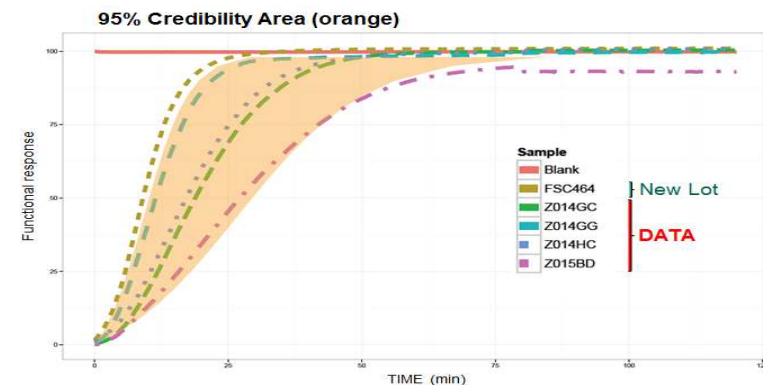
Estimate risks



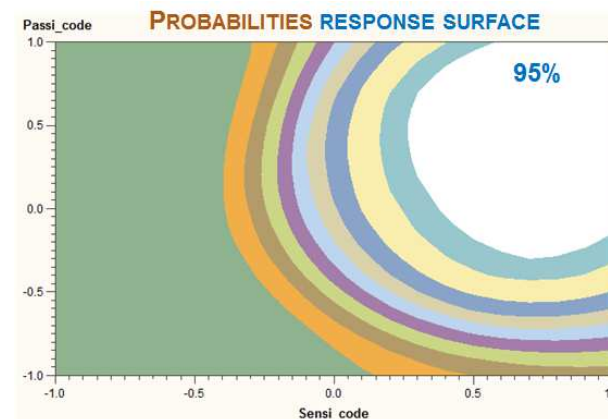
■ Comparison topics

ex: outputs from 2 processes
to be compared

Maximize the use
of information



■ Design Space defined from Design of Experiments



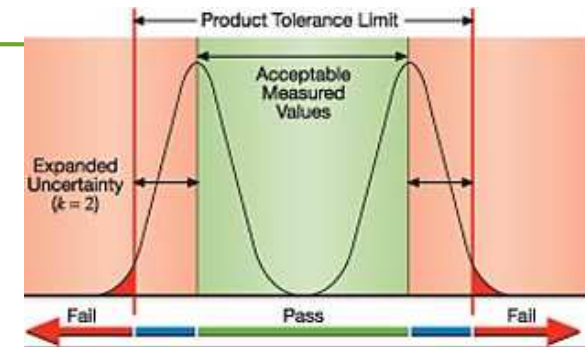
Better control of
variations

Some of the pilot examples (2)

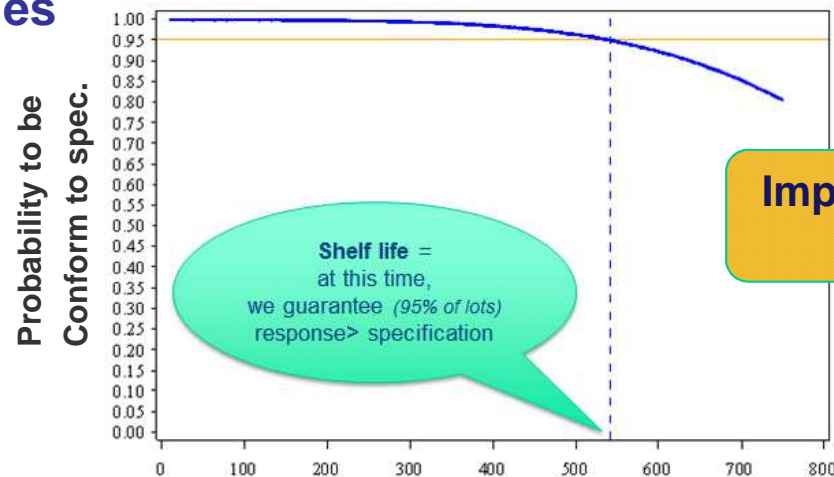
■ Determination of specifications

Tolerance interval

Improve specification setting



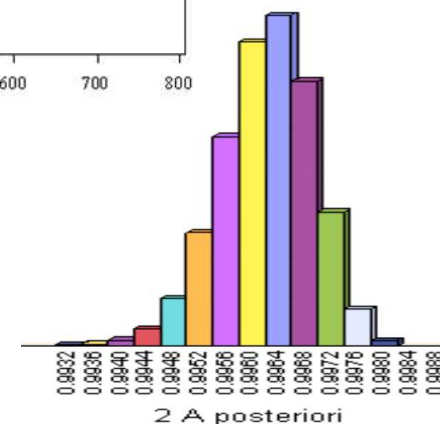
■ Stability Studies issues



Improve performance setting

■ Probability of success of performance studies based on results obtained during development

Better control of risks



Common ways of working for each case

- **Collection of related articles** (*if any*)

- **Practice** on codes and **interpretation** of outputs from Samplers (using  mainly – and )

- **Comparison with frequentist approach**
Added value of Bayesian Statistics

- **Playing with different scenarios:** fix/random effects management, include prior knowledge (more or less), different ways of managing priors...

- I. **Main Statistical Context**
- II. **Project Context**
 - Objective
 - Input Data Description
- III. **Classical Frequentist Approach**
 - Methodology
 - Results & Interpretation
- IV. **Bayesian Approach**
 - Objective
 - Model
 - SAS Code
 - Results & Interpretation
- V. **Frequentist vs Bayesian Fight**
 - Added value of Bayesian (for us/customer)
 - Lesson learned
 - To be continued
 - Open questions

- **Regular meetings** put in place in order to share progress, issues, tips & tricks ...
and maintain **dynamic** within the community

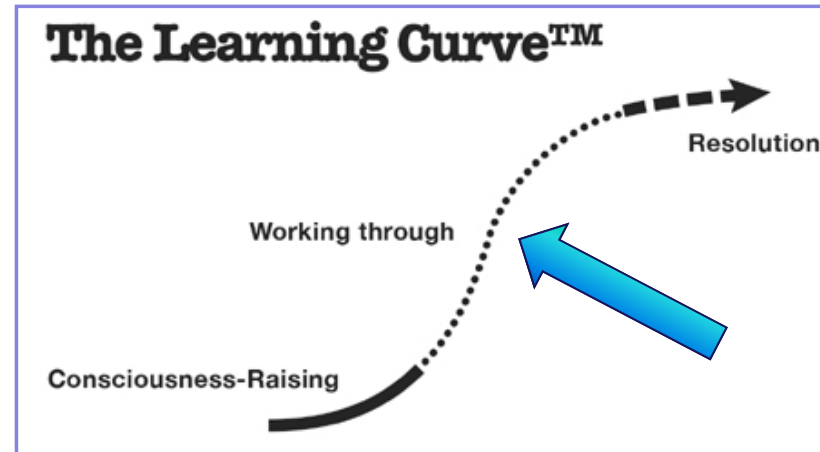
- **Sometimes** calling our favorite coach from  when facing blocking point

Where are we today & next steps

- **Still have a lot to learn.**

BUT, we “significantly” start to change our ways of thinking to better address our customer needs.

We’re less afraid of Bayesian Statistics, even though we still have many issues to deal with!



- **Ready to identify and apply on real cases.**

That’s the priority for the community this year



- We started to **spread out to other BioMaths** (Discovery sessions).

DISCUSSION

➔ **Success factors**



➔ **Issues – Challenges**
Current & futures



Success factors



Proof of added value on one **internal case** (with high business impact) using **external expertise**.



Training session delivered to several BioMaths and directly **followed by internal application** case studies ... to practice and learn



Biomathematics **group size** and **organization** (*functional excellence activities*) to be able to dedicate time on this activity and still “produce”



Regular sharing within community.

Follow-up, success, issues, tips & tricks, ...

Sponsor and protection from the staff



Keep in touch with
Reactivity and excellence of their input
always appreciated

Success factors (2)



- **Tools, rules and team spirit** put in place within the community to facilitate learning & sharing and optimize learning curve.
- **Regular communication on advancement and issues**
- **Motivated team.**
Selection of not too ambitious examples first (quick win)... in order to have success stories and maintain motivation.

Issues - Challenges



- **Maintain** this transversal activity against immediate production needs.
- **Maintain** motivation of the team, and commitment of the staff true success stories.
- **Tools** may be obstacles (SAS version for instance) or lack of practice on R too
- **Technical issues** (still a lot to learn)
- **Ability** to replace “*p-value decision making process*” by **prediction** based-on. Internally first (within BioMaths group) and externally second.

Conclusion



Looking forward to the coming months...



TAKING HEALTH
EVER HIGHER



PIONEERING DIAGNOSTICS

Thank you for your attention





BIOMÉRIEUX



PIONEERING DIAGNOSTICS