STARS
STRENGTHENING
REGULATORY
SCIENCE

The road so far:
Update & spotlight on project activities and results

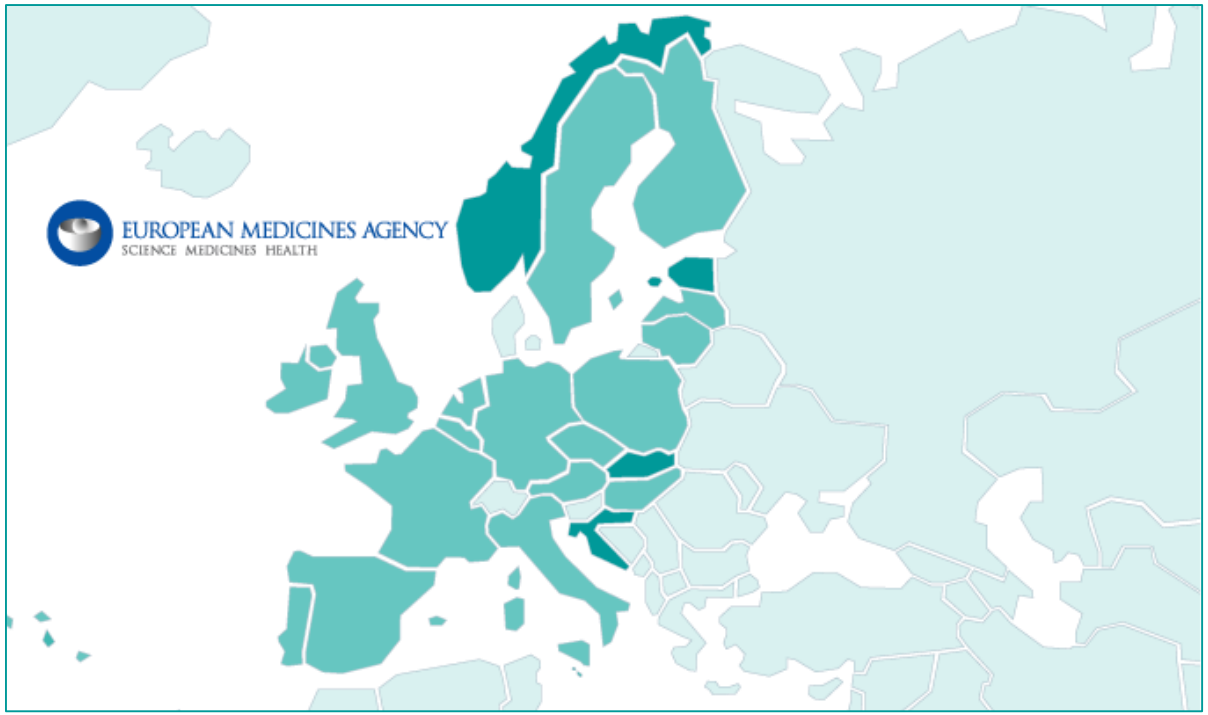
Dr. Wiebke Löbker and Dr. Anne Heß (BfArM)
On behalf of the STARS consortium

Second European Stakeholder Workshop
November 17th/18th,2021

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 825881

CSA-STARS: Strengthening Training of Academia in Regulatory Sciences & Supporting Regulatory Scientific Advice

- Consortium of 21 partners from 18 European countries represented via their NCA & EMA (plus 4 associated partners) and DLR-PT
- Coordination team: BfArM, PEI, DLR-PT (Germany)
- Representatives from EU-Innovation Network
- Funding by European Commission
- Project period: January 2019 – June 2022



Drug Development - From Lab to Patient

Support via SA by NCA

Basic Research → Non-Clinical Research → Clinical Research → Clinical Implementation

PU → Market Access

Deficiency in regulatory knowledge …

… delays the development of new treatment…

… limits the chances that promising innovations will reach patients

Pictures designed by freepik.de

Mind the (Knowledge) Gap

A lot of support activities already exist:

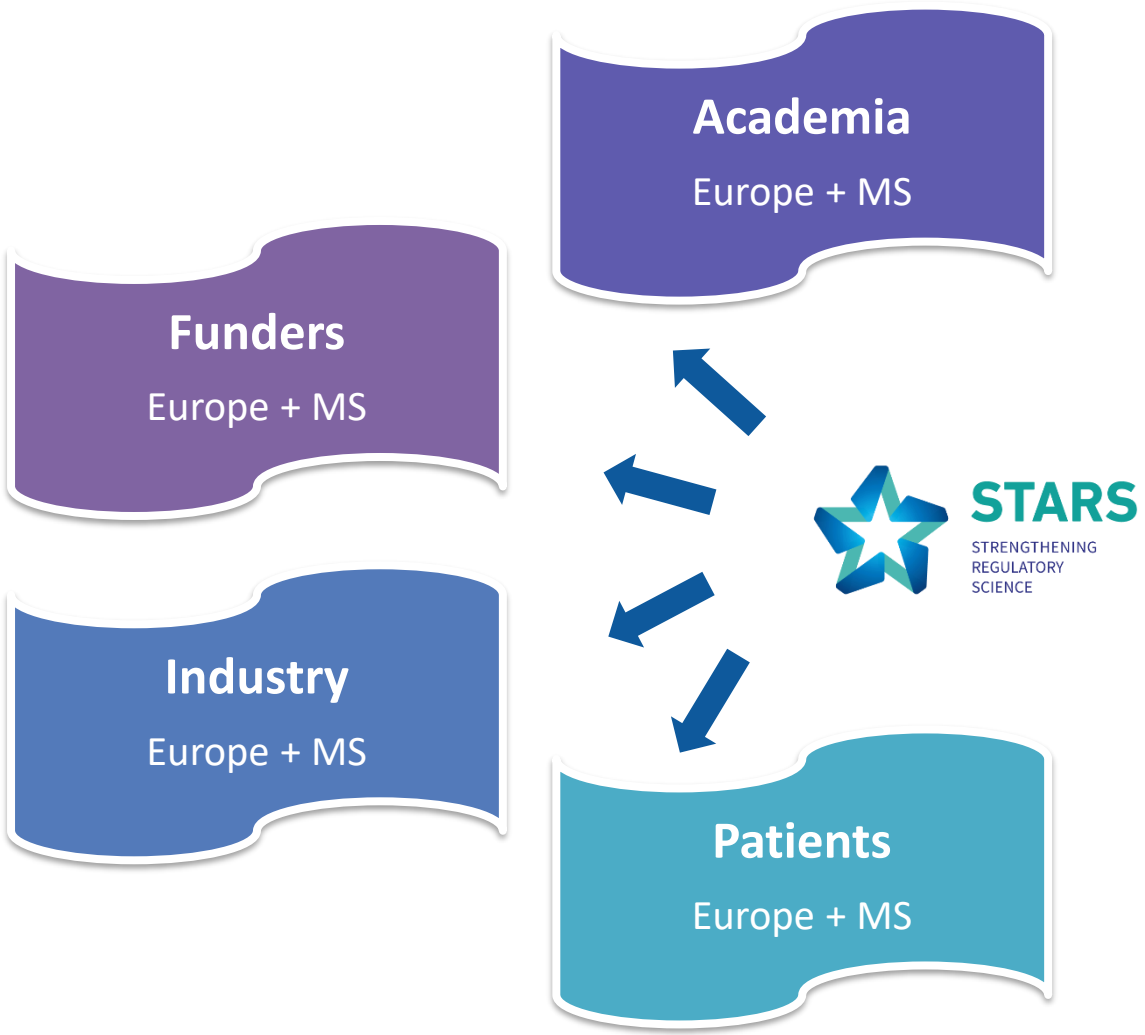
- National level: Scientific Advice, Innovation Offices
- EU level: EMA's early development and advice services (Innovation Task Force, PRIME scheme, SAWP, etc.)
- EU Innovation Network

BUT: barriers/hurdles to make use of them

- Difference in "language", communication between regulator and researcher
- Lack of awareness
- "Respect" towards the authority
- Limited knowledge → Difficulties to ask the right questions at the right time
- …

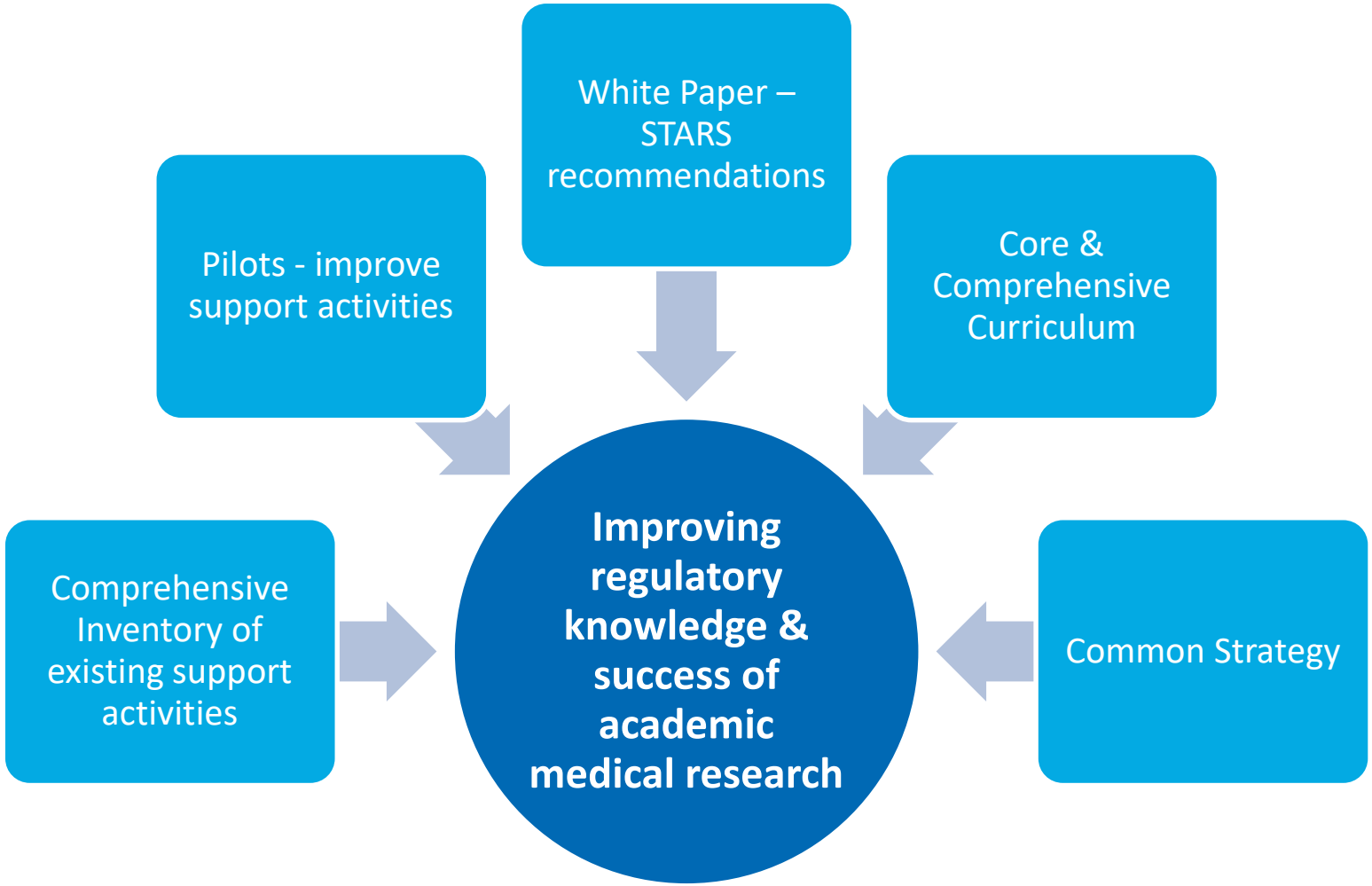
Major Goals of STARS

Interactions with Stakeholders –Communication is Key!



- WP1: Project Management
- WP2: Surveys and Inventory
- WP3: Curricula and Strategy
- WP4: Pilots
- WP5: Recommendations
- WP6: Communication and Dissemination

Working Programme, Project Outcomes and Impact



The STARS Road so far…

STARS Kick-Off Meeting

Jan 2019

STARS Surveys
- Academia
- Funders
- NCAs/EMA

Jun-Sep 2019

Launch of Comprehensive Inventory v1

Sep 2020

White Paper
- Analysis of gaps and recomm.

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- Identified Gap
- Curriculum

Core & Comprehensive Curriculum

Draft of Common Strategy

STARS Surveys

Data Basis for STARS Activities

Research Groups & Research Centers

- Awareness/usage of regulatory guidance and support
- Challenges in regulatory matters for academic researchers
- Training needs

Funding Bodies

- Consideration and requirements of regulatory aspects
- Contact with regulatory authorities
- Coverage of costs for Scientific Advice

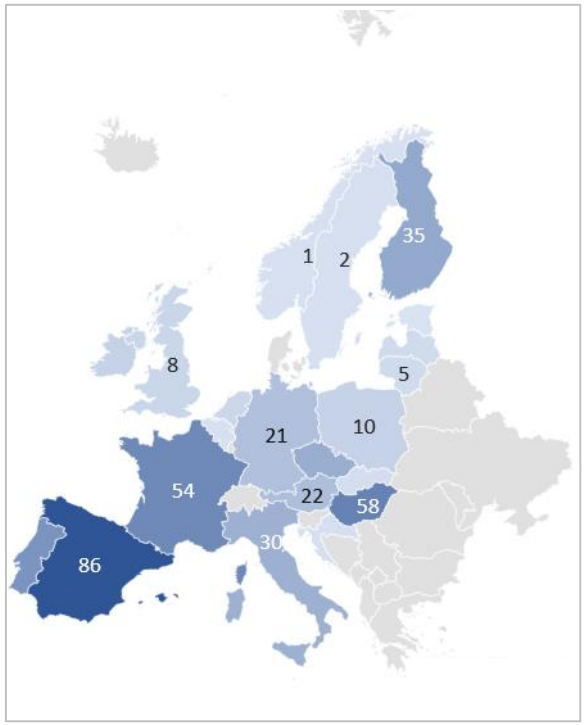
Regulatory Agencies in EU

- Preparedness of academia requesting Scientific Advice
- Experience with academia in Scientific Advice
- Regulatory training and regulatory support offered

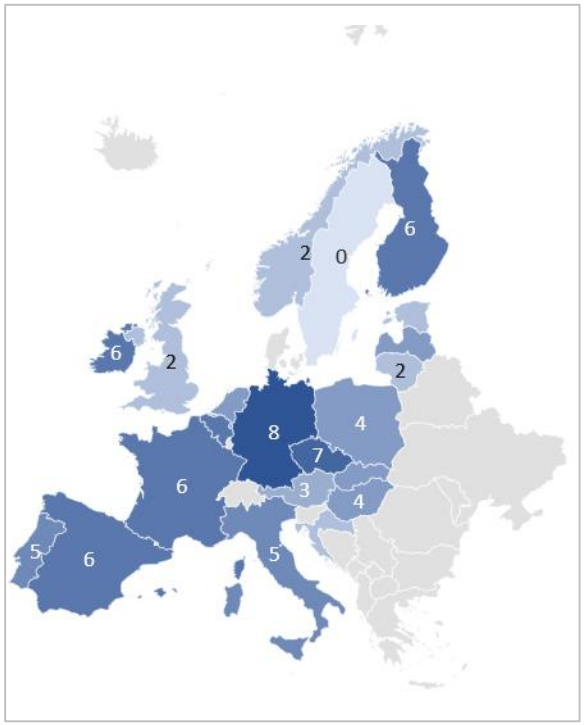
Kallio et al., manuscript in preparation

STARS Surveys

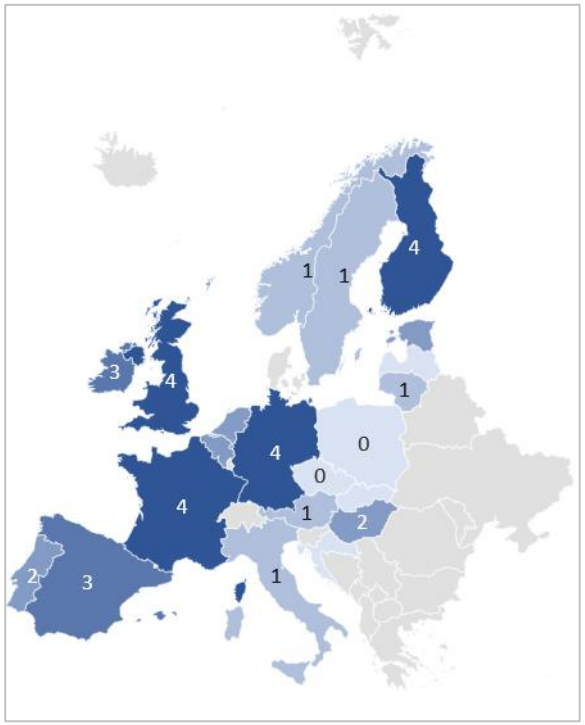
Data Basis for STARS Activities



Research groups (n=449)



Research centers (n=88)

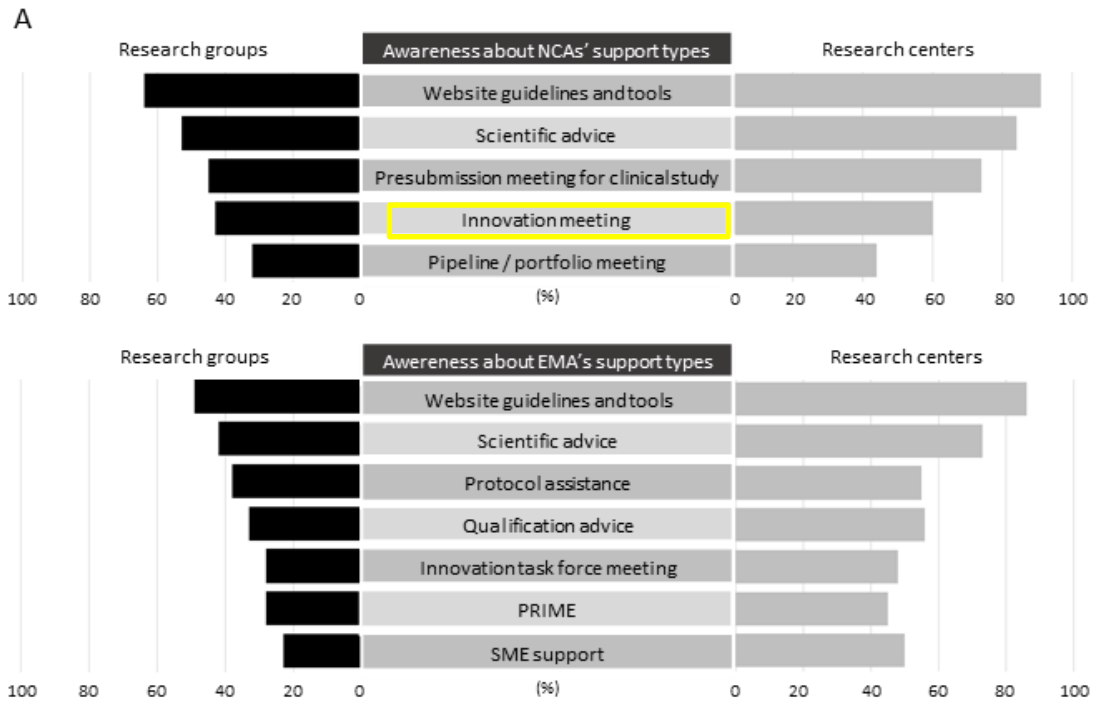


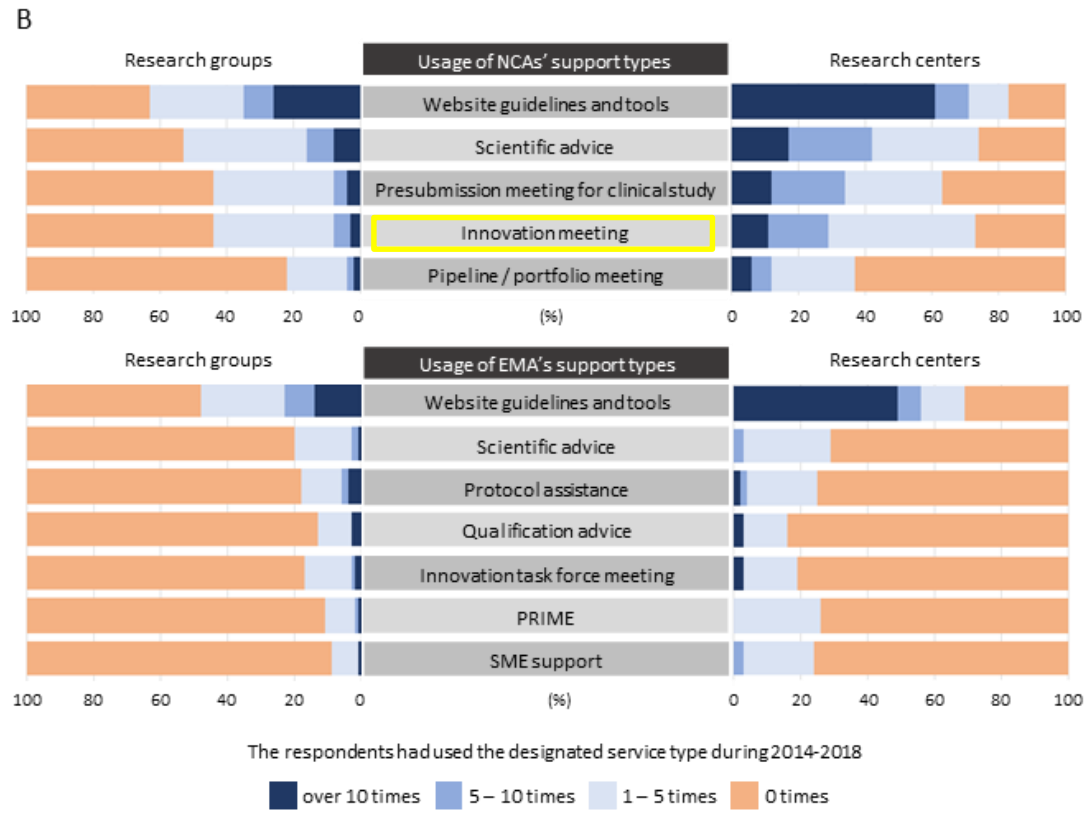
Funding organisations (n=40)

NCAs (n=21)

STARS Surveys

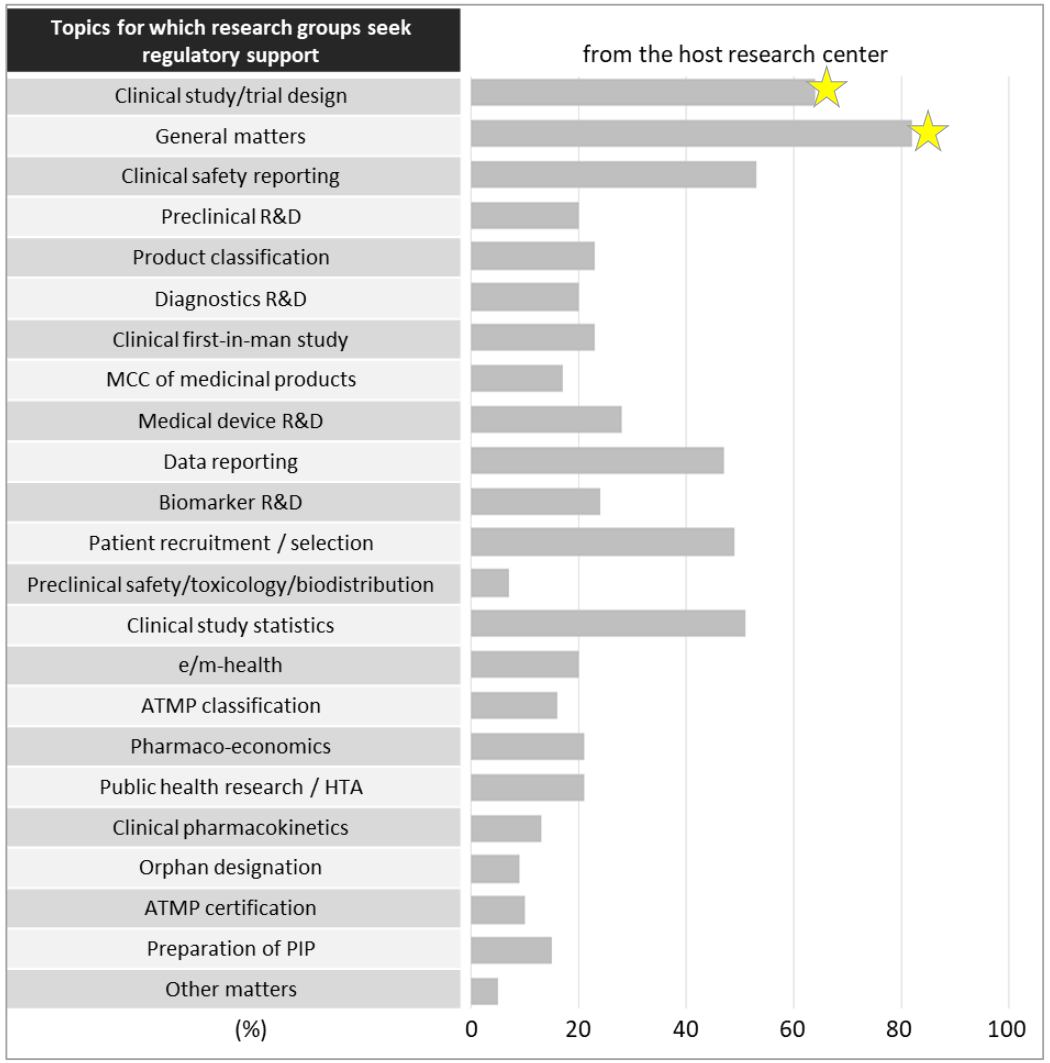
Awareness and Usage of Regulatory Rupport





Kallio et al., manuscript in preparation

STARS Surveys
Topics, challenges, gaps



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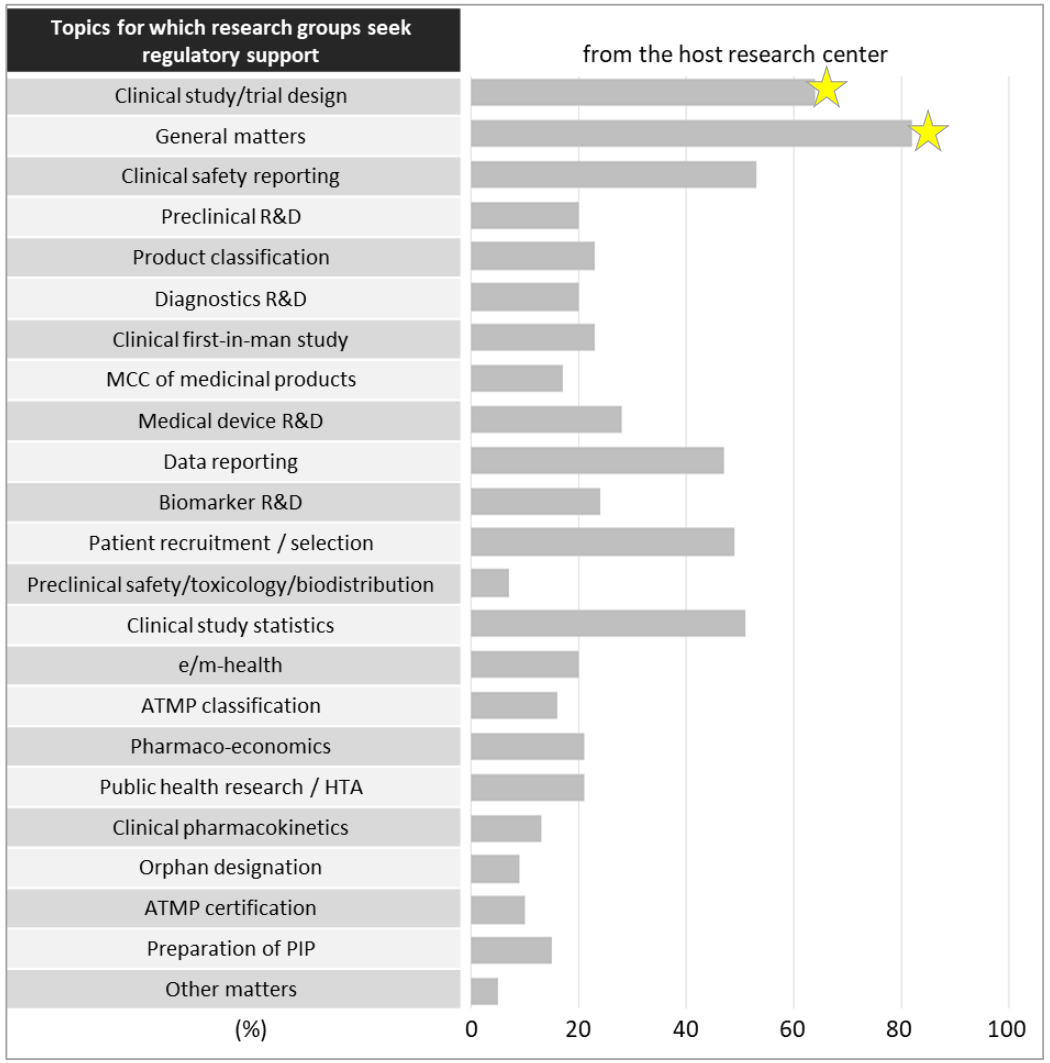

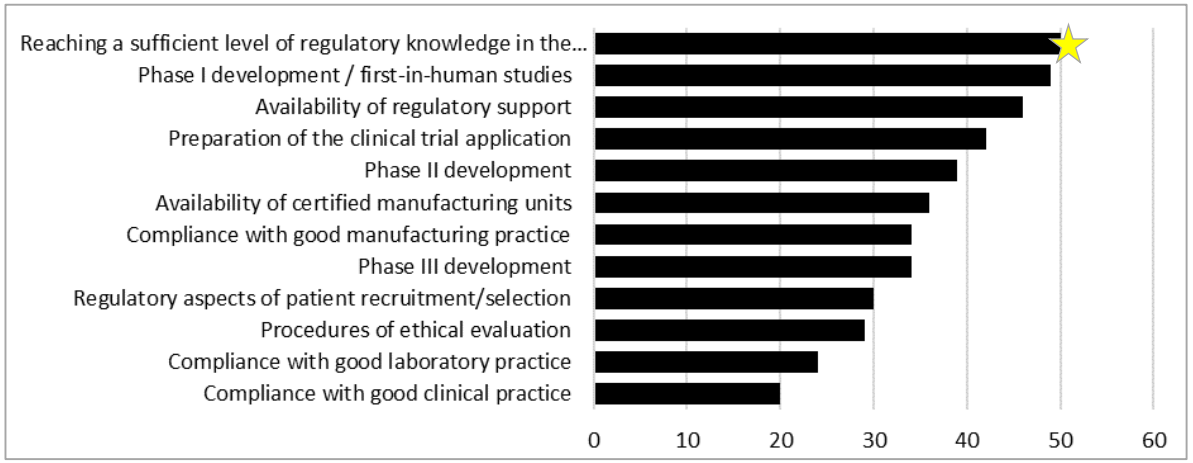

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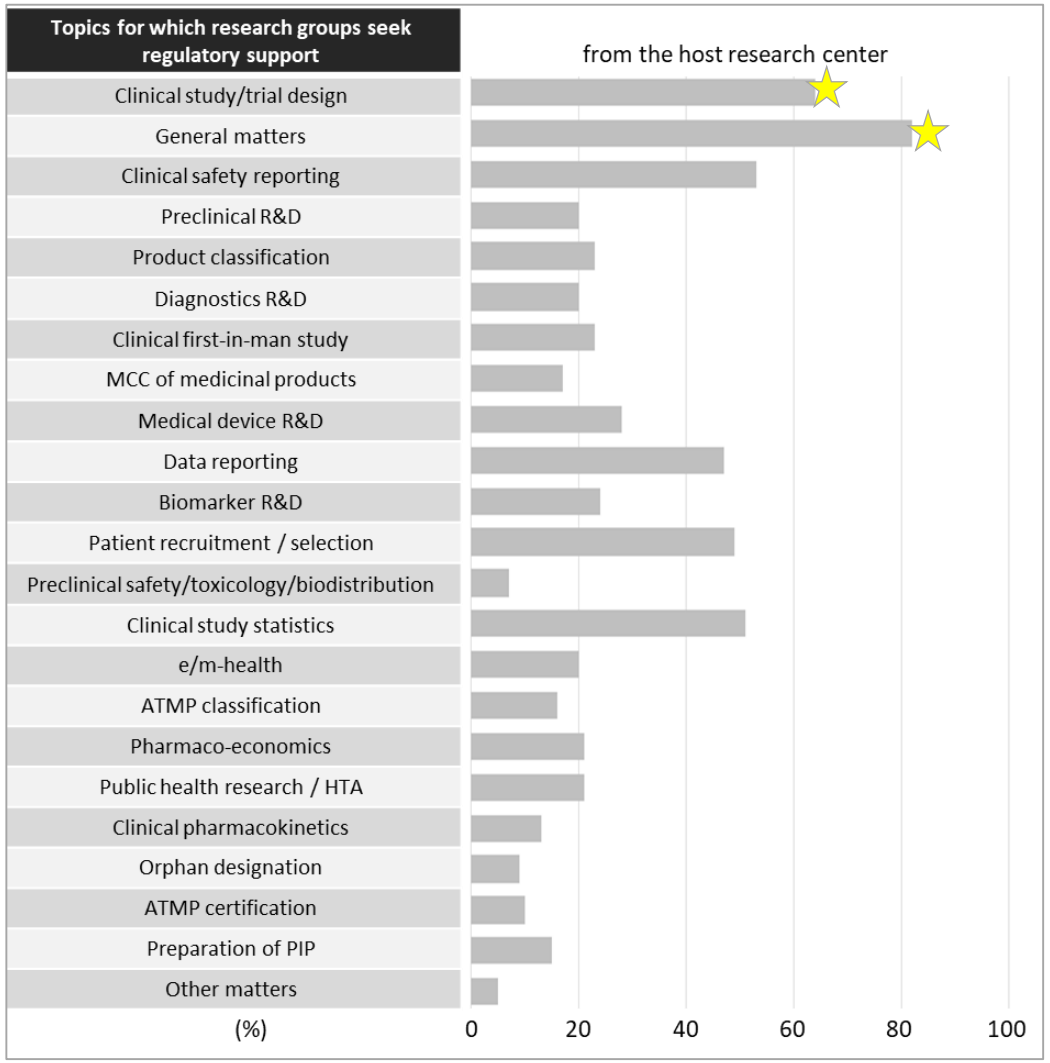

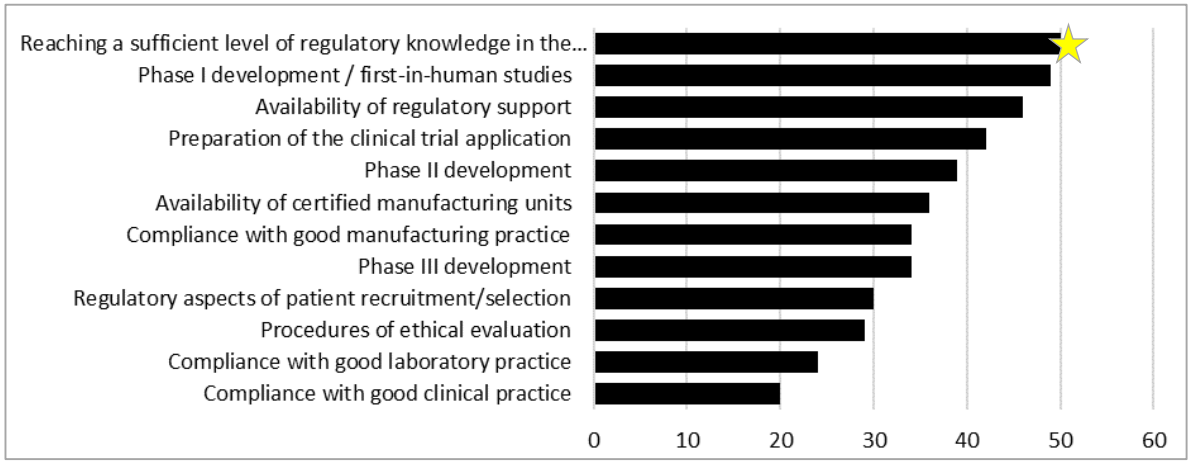

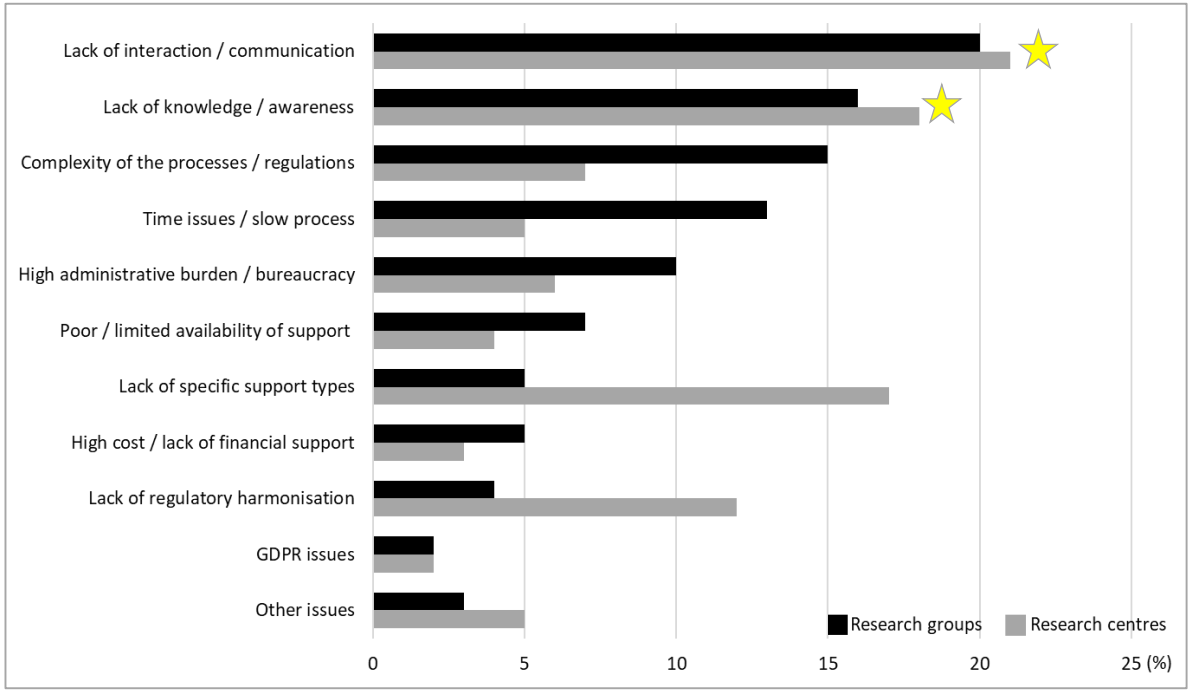

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Draft of Common Strategy

Comprehensive Inventory (CI)

Comprehensive overview of support services for regulatory activities

Listing by Expertise Area

Country	Provider Type	Expertise	Provider Details
Spain	National Competent Authority	ATMPs	AEMPS
Belgium	Public Actor	ATMPs	Antwerp University Hospital
France	Public Actor	ATMPs	AP-HP
Germany	Public Actor	ATMPs	Association for Applied Human Pharmacology
Austria	National Competent Authority	ATMPs	BASG / AGES
France	Public Actor	ATMPs	CHU Amiens Picardie
Spain	Public Actor	ATMPs	CIBER
Switzerland	Public Actor	ATMPs	Clinical Trails Center Zurich
Germany	Public Actor	ATMPs	Clinical Trial Centre Leipzig
Europe	Public Actor	ATMPs	Coordination Centre for Clinical Trials (KKS) Heidelberg
Germany	Public Actor	ATMPs	Coordination Centre for Clinical Trials (KKS) Heidelberg
Czech Republic	Public Actor	ATMPs	Czech Clinical Research Infrastructure Network
Europe	Public Actor	ATMPs	EATRIS

Listing by Support Scope

Country	Provider Type	Support Activity	Provider Details
Portugal	Public Actor	Assistance in clinical trial application	2CA-Braga
Spain	National Competent Authority	Assistance in clinical trial application	AEMPS
Belgium	Public Actor	Assistance in clinical trial application	Antwerp University Hospital
France	Public Actor	Assistance in clinical trial application	AP-HP
Germany	Public Actor	Assistance in clinical trial application	Association for Applied Human Pharmacology
Austria	National Competent Authority	Assistance in clinical trial application	BASG / AGES
Germany	National Competent Authority	Assistance in clinical trial application	BfArM
Ireland	Public Actor	Assistance in clinical trial application	Cancer Trials Ireland
Germany	Public Actor	Assistance in clinical trial application	Center for Clinical Trials Tuebingen
France	Public Actor	Assistance in	CHU Amiens Picardie

Direct support for clinical researcher!
Visit our website:
https://www.csa-stars.eu/Inventory-1721.html

Comprehensive Inventory

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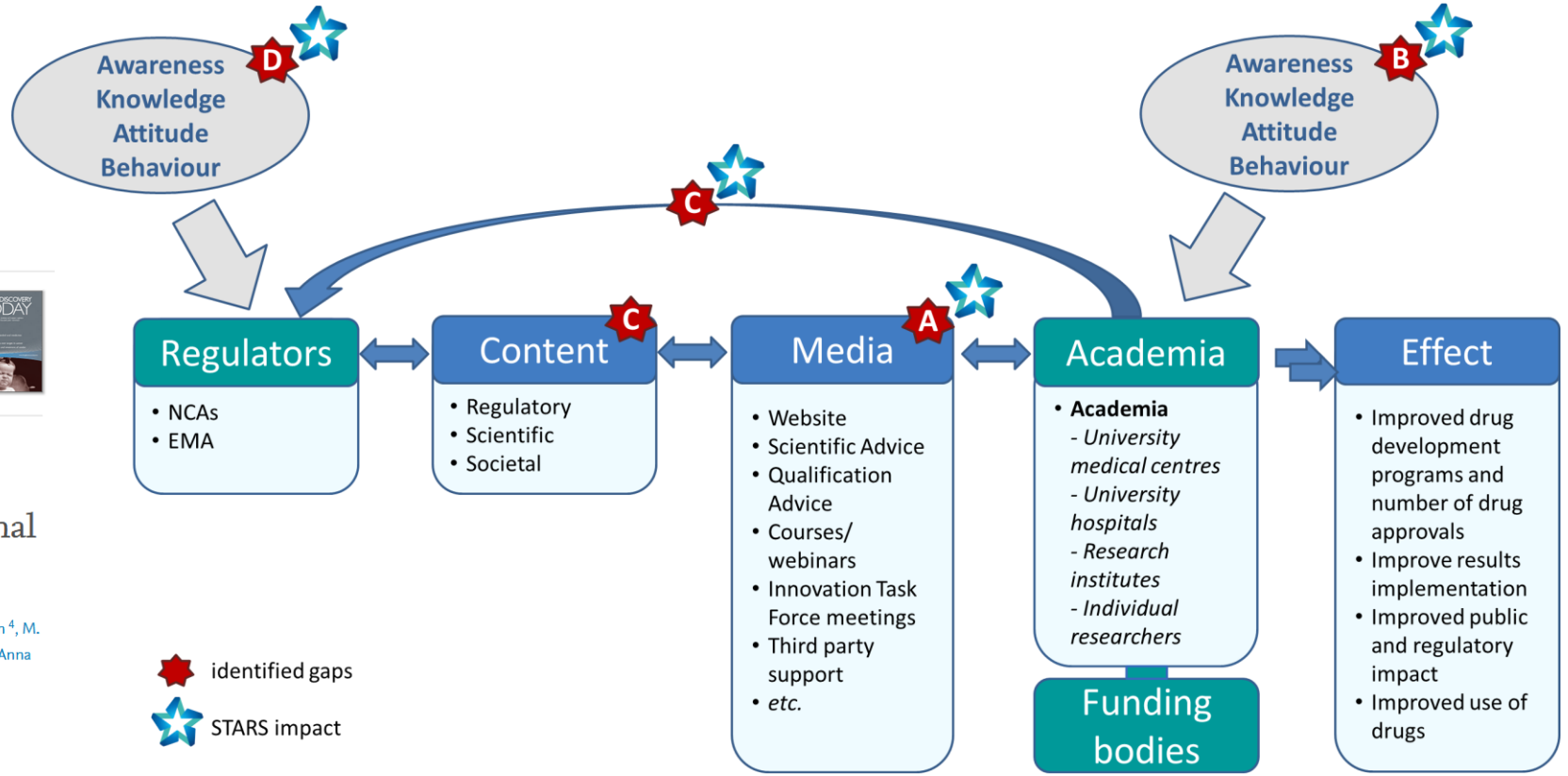
STARS White Paper

Communication & Interaction Framework and its Gaps



Drug Discovery Today
Volume 26, Issue 2, February 2021, Pages 283-288

Feature

Strengthening regulatory science in academia: STARS, an EU initiative to bridge the translational gap

Viktoriia Starokozhko [1, 2], Marko Kallio [3], Åsa Kumlin Howell [4], Anna Mäkinen Salmi [4], Gunilla Andrew-Nielsen [4], M. Goldammer [5], Manja Burggraf [6], Wiebke Löbker [7], Anne Böhmer [7], Eleonora Agricola [8], Corinne S. de Vries [9], Anna M.G. Pasmooij [1], Peter G.M. Mol [1, 2], on behalf of the STARS consortium

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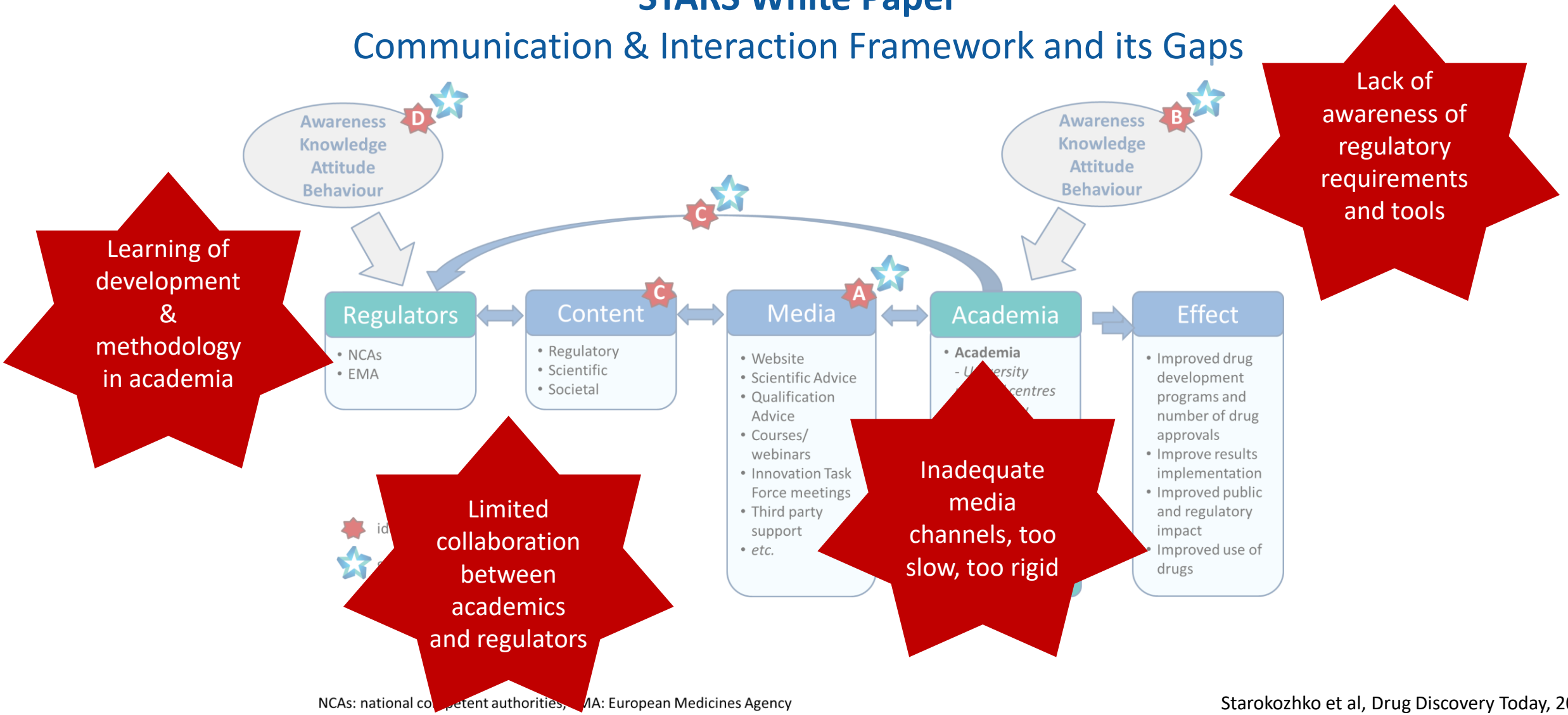
https://doi.org/10.1016/j.drudis.2020.10.017

NCAs: national competent authorities; EMA: European Medicines Agency

Starokozhko et al, Drug Discovery Today, 2021

STARS White Paper

Communication & Interaction Framework and its Gaps



NCAs: national co petent authorities, MA: European Medicines Agency

Starokozhko et al, Drug Discovery Today, 2021

Key Steps Towards Improving Regulatory Dialogue

Changing the Mindset

Implementation of regulatory science in educational programmes of medical, biomedical and pharmaceutical professionals

Proactive communication with regulatory authorities and funding bodies throughout development

Active dialogue versus one-way communication, open-minded communication

Interest in a more-defined public impact of funded research projects

Scrutinize grant proposals in the area of applied and translational research for the adoption of best practices

Continuous learning about upcoming innovative therapies through knowledge exchange with academia

Groups:

- Academia
- Funding Bodies
- Regulators

1st European Stakeholder Workshop

Changing the Mindset

Implementation of regulatory science in educational programmes of medical, biomedical and pharmaceutical professionals

Active dialogue versus one-way communication, open-minded communication

Proactive communication with regulatory authorities and funding bodies throughout development

Aim:

Exchange with the **research community** and **important stakeholders** on how to change the mindset

Major outcomes:

- **Bridging the language gap**
- **Bidirectional communication**
- **Continuous regulatory training**

about upcoming innovative therapies through knowledge exchange with academia

Scrutinize grant proposals in the area of applied and translational research for the adoption of best practices

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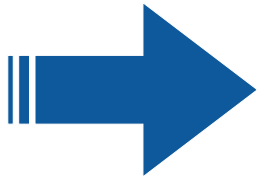
- Pilot I: Transfer of an identified **best practice example** to (an) other EEA member states
- Pilot II: Addressing gaps – initiation of a **novel support activity** for improving success on regulatory Scientific Advice
- Pilot III: Implementing the Comprehensive Curriculum

Pilot I - Background

Transfer of an identified best practice example

STARS survey data:

- The aim/motivation of academia for contacting the NCAs for Scientific Advice is **clinical trial design** (46%) and **general regulatory matters** (40%)
- Topic on training needs with the highest rank was **clinical study protocol** (52%)
- Most challenging: reaching sufficient level of regulatory knowledge



Unmet need for a basic training on **essential regulatory knowledge** for researchers in the academic

Pilot I - Concept

Transfer of an identified best practice example + evaluation

Provider:
NL and CZ Partner

Best practice
Regulatory Training Course

Transfer

Evaluation

Recipient:

Austria
Hungary
Italy

Pilot I - Realisation

Transfer of an identified best practice example

The Winding Road from a Brilliant Idea to Drug Approval
February 23 - 26, 2021

Program

Day 1 – 23. 02. 2021	
10:00.10:20	Opening - Introduction to Pilot Course (STARS team)
10:20-12:20	F-I-H sponsor – investigator - Clinical trial site (Eva Hruskova Reinova)
12:20-12:30	Q&A (Clinical)
12:30-12:50	Coffee Break
12:50-13:50	Non-clinical research – KEY MILESTONE in the Drug developent (Eva Kolouchova)
13:50-14:00	Q&A (Non-clinical)

Day 2 – 24. 02. 2021	
10:00-11:10	IMPD – regulatory quality requirements/ Regulatory perspectives on quality requirements of biological products (Ivana Pravdova, Barbora Ladinova)
11:10-11:20	Q&A (Quality)
11:20-11:40	Coffee Break
11:40-12:30	Advanced Therapy Medicinal products (ATMP) (Tomas Boran)
12:30-13:45	Advanced therapy medicinal products ATMP – from science to clinical trial Requirements on quality (Ivana Haunerova)
13:45-14:00	Q&A (ATMP)

Day 3 – 25. 02. 2021	
09:00-09:30	Introduction to Day 3. How regulators work and think: the basics (Peter Mol)
09:30-09:35	Q&A
09:35-10:05	Novel regulatory tools & drug development support mechanisms (Peter Mol)
10:05-10:10	Q&A
10:10-10:25	Coffee break
10:25-10:50	Scientific advice (European & national) (Marjon Pasmooij)
10:50-10:55	Q&A
10:55-11:20	Case example – ATMP scientific advice (Viktoriia Starokozhko)

11:20-11:25	Q&A
11:25-11:40	Coffee break
11:40-12:10	Novel methodologies and Real World Evidence supporting drug regulatory decision-making
12:10-12:30	Final Q&A round (Moderator: Marjon Pasmooij)

Day 4 – 26. 02. 2021	
10:00-10:10	Introduction to the Q& A session, introduction of the regulatory representatives (Peter Mol)
10:10-12:00	Q&A - Moderator Peter Mol

Topics of the online course:

- Essential regulatory knowledge in drug development
- Specific Regulatory Knowledge for Advanced Therapy Medicinal Products (ATMPs)
- Regulatory system and framework

Pilot I - Evaluation

I would include more information about clinical trials regulatory issues

Workshop on how to write a preclinical/clinical proposal.

Maybe you can repeat this course again, from time to time

I would like that every young oncologist would attend this kind of courses.

regular update on applicale new regulations and laws

Was the language understandable?

75%: very understandable

25%: abbreviations not understandable

Would you recommend the course to others?

94%:

6%:

Pilot I - Conclusion

- Audience was satisfied in all respects (content, length and format)
- Importance and applicability of such a training course was acknowledged
- Course content and format was acknowledged
- Regular training, going into more details, with more interactive part would be considered as very useful and supportive
- Conclusions/outcome will fit into STARS Common Strategy

The course materials are published online!
Visit our website:
https://www.csa-stars.eu/Results-Pilot-I-Best-Practice-Transfer-1754.html

Slides of the Online Training Course

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- Pilot III: Implementing the Comprehensive Curriculum

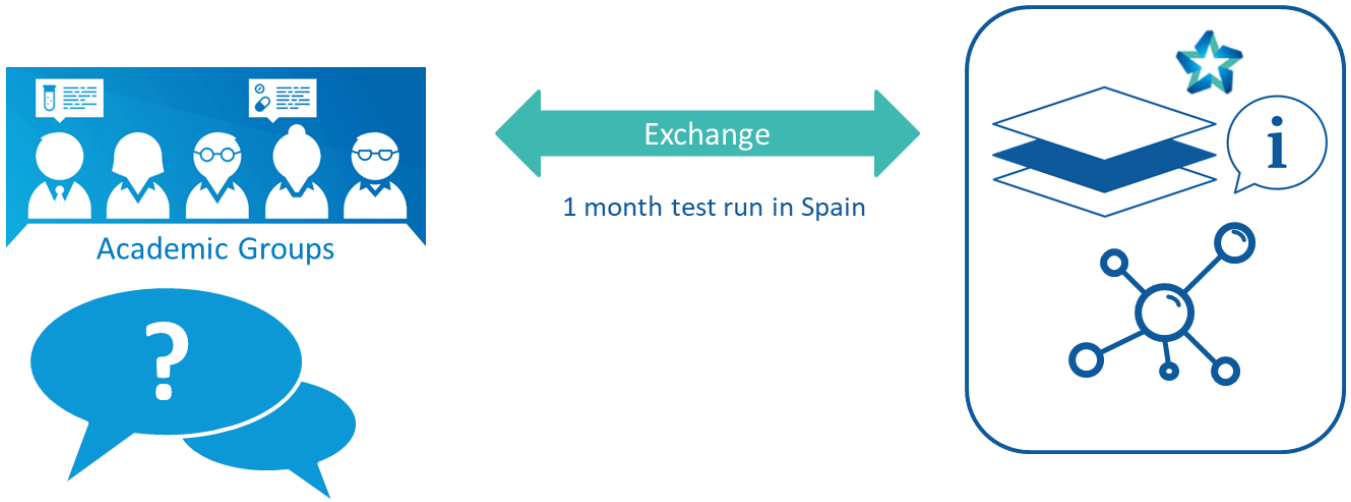
Pilot II

Initiation of a Novel Support Activity

STARS Survey data:

- Tool/s to improve the communication between regulators and academia
- Timely response is probably the most remarkable need

Concept: one-stop-shop platform for Spanish academia



Pilot Project II

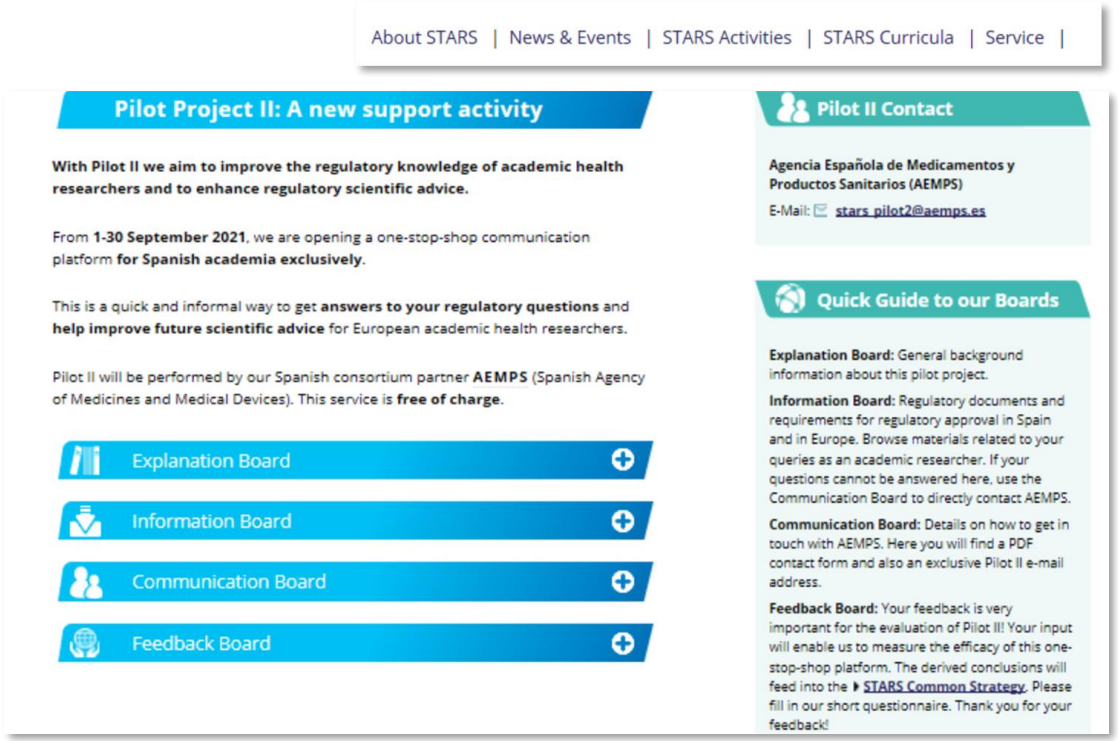
Initiation of a novel support activity for improving success on regulatory Scientific Advice.

- Explanation Board
- Information Board
- Communication Board
- Feedback Board

Pilot II

Initiation of a Novel Support Activity

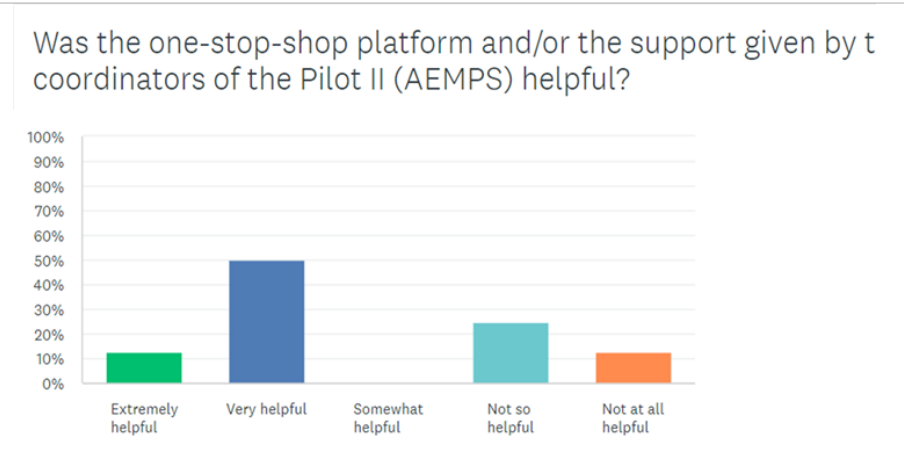
- Carried out by AEMPS in Sep. 2022



Documents and Information:

→ Relevant documents (scientific guidelines, ICH guidelines, presentations, etc.)

Pilot II – Preliminary Results of Pilot Evaluation



Continue with this platform

Include live sesssions

Add short videos explaining the trajectory of an idea to final approval

Establish a communication system for feedback responses and doubts.

Short video "pills" with principal ideas and concepts

Pilot II

Initiation of a Novel Support Activity

Documents are published online!
Visit our website:
https://www.csa-stars.eu/Pilot-Project-II-Information-Board-1749.html#regulatory

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STARS Curricula

Background and Data Basis for Development

To achieve a harmonised and common level of regulatory knowledge

Not to substitute or replace any existing curricula in the EU, but to identify and to address current gaps

To meet the different needs and requirements of the national education systems

STARS Curricula

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To meet the different needs and requirements of the national education systems

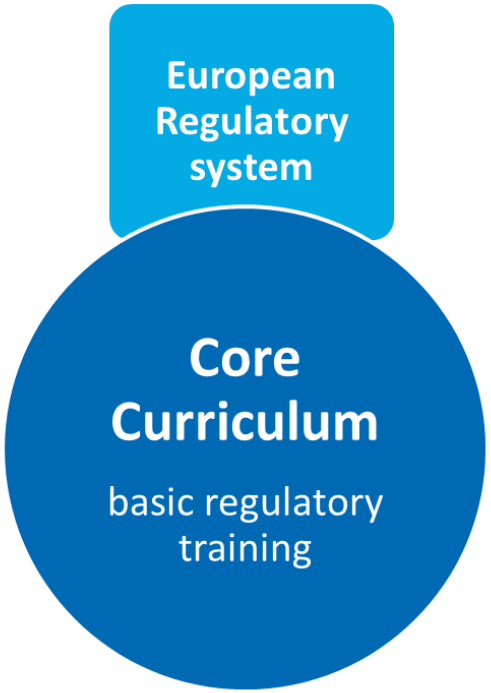
NCAs survey results

- Analysis of training offered to graduate students, post-graduate students and healthcare professionals
- Top 3 training topics: pharmacovigilance; regulatory system/legislation; clinical studies
- Top activities and materials offered: lectures and guidelines
- Strong recommendation to include the “Regulatory system/legislation” topic in any educational support activities

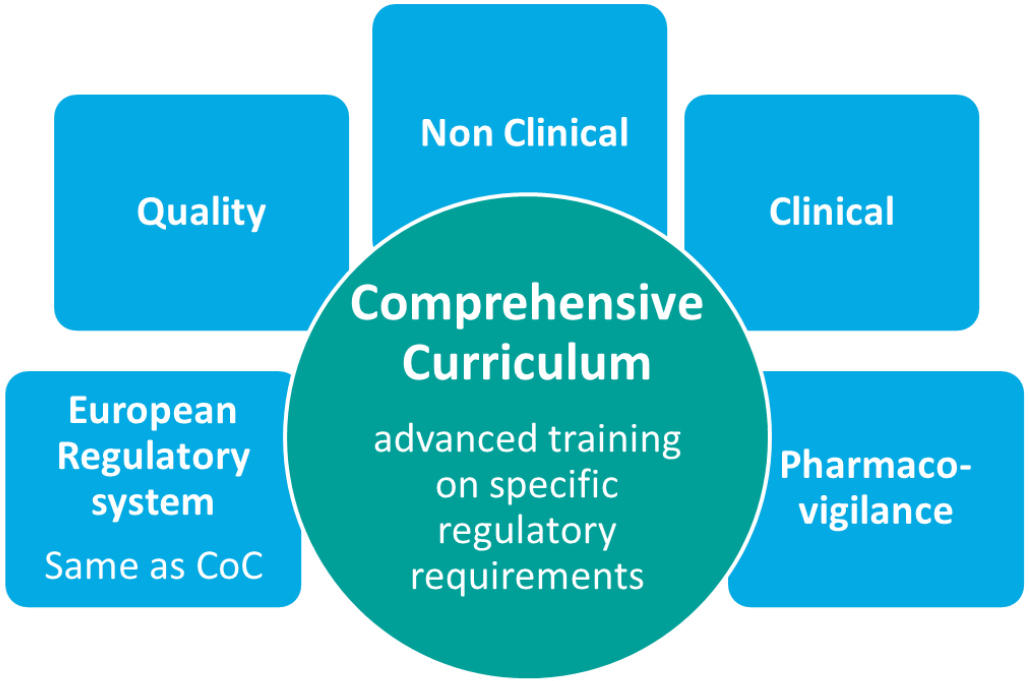
1st European stakeholder workshop

- Lack of basic regulatory knowledge
- Proposal for “train the trainer” concept as an appropriate strategy
- Proposal for a harmonised and standardised approach to establish a modular system for basic regulatory education
- Consensus on the need of special training at a deeper level regarding some challenging topics.

STARS Curricula



Bachelor and Master's students



Healthcare professionals

Core Curriculum on European Regulatory System

- EU Regulatory bodies and their roles/activities
- Pharmaceutical legal framework
- Pharmacovigilance in EU
- Regulatory activities of EMA and NCAs in support of innovation, research and product development
- Phases of clinical trials and the level of quality/non-clinical/clinical evidence required
- EU marketing authorization procedures
- Post-marketing phase
- Medicines and medical devices
- Early access tools

Comprehensive Curriculum

Quality

- Principles and guidelines applying to the pharmaceutical development
- The specific regulatory framework to address quality requirements in the relevant field of study, considering those which are particular to the specific product of interest
- Quality requirements for investigational medicinal products
- CTD modules 1, 2 and 3
- EU legal framework and national implementation of GMP, role and scope of GMP inspections
- European pharmacopeia structure and relevant monographs
- From assessment to product information

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Non-Clinical

- Principles and guidelines applied to the non-clinical development
- CTD modules 1, 2 and 4
- Proof of principle: in vitro and in vivo studies addressing PD activity
- Pre-clinical studies to support first in human (FIH) study
- Establishing the clinical dose
- Non-clinical studies to support MAA
- Importance of animal species selection
- Alternative approaches to animal model
- Basic principles of GLP
- Basic principles of environmental risk assessment
- Studies in juvenile animals to support pediatric use
- Regulatory and scientific requirements for non-clinical development
- Integration of non-clinical results with quality and clinical data
- From assessment to product information

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- Alternative approaches to animal model
- Basic principles of GLP
- Basic principles of environmental risk assessment
- Studies in juvenile animals to support pediatric use
- Regulatory and scientific requirements for non-clinical development
- Integration of non-clinical results with quality and clinical data
- From assessment to product information

Clinical

- Clinical trial legislation in the EU, GCP, declaration of Helsinki and ethical principles, relevant guidelines
- CTA
- EU clinical trials information system
- Pharmacovigilance in clinical trials
- Overview of scientific guidelines
- CTD modules 1, 2 and 5
- Structure and content of clinical study report
- Real word data and patient registries
- Paediatric medicines
- Orphan medicines
- ATMPs
- Vaccines
- Biosimilars, generics and hybrid applications
- From assessment to product information

Comprehensive Curriculum

Quality

- Principles and guidelines applying to the pharmaceutical development
- The specific regulatory framework to address quality requirements in the relevant field of study, considering those which are particular to the specific product of interest
- Quality requirements for investigational medicinal products
- CTD modules 1, 2 and 3
- EU legal framework and national implementation of GMP, role and scope of GMP inspections
- European pharmacopeia structure and relevant monographs
- From assessment to product information

Non-Clinical

- Principles and guidelines applied to the non-clinical development
- CTD modules 1, 2 and 4
- Proof of principle: in vitro and in vivo studies addressing PD activity
- Pre-clinical studies to support first in human (FIH) study
- Establishing the clinical dose
- Non-clinical studies to support MAA
- Importance of animal species selection
- Alternative approaches to animal model
- Basic principles of GLP
- Basic principles of environmental risk assessment
- Studies in juvenile animals to support pediatric use
- Regulatory and scientific requirements for non-clinical development
- Integration of non-clinical results with quality and clinical data
- From assessment to product information

Clinical

- Clinical trial legislation in the EU, GCP, declaration of Helsinki and ethical principles, relevant guidelines
- CTA
- EU clinical trials information system
- Pharmacovigilance in clinical trials
- Overview of scientific guidelines
- CTD modules 1, 2 and 5
- Structure and content of clinical study report
- Real word data and patient registries
- Paediatric medicines
- Orphan medicines
- ATMPs
- Vaccines
- Biosimilars, generics and hybrid applications
- From assessment to product information

Post-marketing

- Pharmacovigilance legislation, GVP, relevant guidelines
- Collection and management of suspected adverse reactions
- Risk Management Plan
- PASS, PAES and other post-authorisation activities
- Risk Minimisation Measures
- Pharmacovigilance systems
- Signal management
- Overview and assessment
- of PSURs
- Referrals for safety reasons
- Renewals and annual re-assessment
- Safety communication

The STARS Road so far…

STARS Kick-Off Meeting

Jan 2019

STARS Surveys
- Academia
- Funders
- NCAs/EMA

Jun-Sep 2019

Launch of Comprehensive Inventory v1

Sep 2020

White Paper
- Analysis of gaps and recomm.

1st European Stakeholder Workshop

Nov 2020

STARS Pilots
- Best Practice
- Identified Gap
- Curriculum

Core & Comprehensive Curriculum

Draft of Common Strategy