EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Regulatory Science

Research needs

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SCIENCE MEDICINES HEALTH

13 December 2021
EMA/705364/2021
Regulatory Science and Innovation

Regulatory Science Research Needs (version 1.0)

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Executive summary

Gaps exist in regulatory science that need to be addressed to improve medicine development and evaluation, ultimately to enable access to innovative medicines that address patients' needs. The European Medicines Agency (EMA) identified around one hundred topics, published here as the 'Regulatory science research needs' list.

By publishing this list, the Agency hopes to stimulate researchers and funding organisations to consider addressing these needs in their work and programmes. The list will be updated periodically with new topics and references to related research.

The acceleration of innovation in medicines development requires a parallel advancement in regulatory science. New technologies and evolving science throw up new regulatory questions and it is important that these questions are answered so that innovation is translated safely and swiftly into effective, high-quality therapies[1]. Answering these questions, and advancing regulatory science, requires research in areas where regulators see the public health need and where collaboration between regulators and other stakeholders is required.

To advance regulatory science research, the Agency committed to convey the regulatory science research needs (RSRN) in its Regulatory Science to 2025 strategy (RSS).[1,2] Specifically it committed to 'Develop network-led partnerships with academic/research centres to undertake research in strategic areas of regulatory science' and to 'Leverage collaborations between academia and network scientists to address rapidly emerging regulatory science research questions' and this was subsequently reinforced in the European Medicines Regulatory Network (EMRN) Strategy to 2025 and is now also a key element in the EMA programming document 2021-2023.[3]

Addressing the research needs in regulatory science requires a collaboration with both academia and key research funding bodies. While EMA may be able to fund a small portion of the research needs, external funding obtained by researchers will remain the primary pathway for addressing the research topics. To this end, EMA is committed to fostering a strong working relationship with European academicians and researchers as well as key research funding bodies, as part of the EMA's Academia Action Plan.[4]

Regulatory science research needs

The regulatory science research needs list emerged from the stakeholder consultations which underpinned the Regulatory Science Strategy to 2025.[2] Interviews were carried out with chairs of the Agency's scientific committees and working parties together with external experts and key opinion leaders from principal stakeholder groups. Many of these identified specific topics for regulatory science research to fill knowledge gaps.

The needs concern research in a broad range of regulatory science topics. In 2021, the Agency validated the research needs list with the academia collaboration matrix, the Healthcare Professionals' Working Party, the Patients' and Consumers' Working Party and the scientific committee chairs, resulting in a list of around one hundred topics for research into regulatory science for human and veterinary medicines.

[1] https://doi.org/10.1111/bcp.14099
[2] https://www.ema.europa.eu/en/about-us/how-we-work/regulatory-science-strategy
[3] https://www.ema.europa.eu/en/documents/report/final-programming-document-2021-2023_en.pdf
[4] https://www.ema.europa.eu/documents/other/academia-collaboration-matrix-action-plan-2021-2023_en.pdf

Addressing these research needs will help advance regulatory science to keep pace with evolving technologies and improve patient access to medicines. Academic researchers and funders are therefore encouraged to consider addressing these needs in their work and programmes.

Why engage on regulatory science research needs?

The regulatory science research needs reflect a clear public health need based on regulatory experience, and generating knowledge to close any of these gaps can have a direct impact on public health by helping the Agency to improve scientific guidelines and regulatory decision-making.

The added value of engaging on these regulatory science research needs includes:

- Translation of results into regulatory practice through informing scientific guidelines, and therefore impacting medicine development and public health
- Dissemination of results via Agency events, discussions with regulatory scientists in the EU network and joint publications with regulatory scientists
- Enabling contribution to evaluations and discussions of specific products, qualifications or guidelines
- Influencing future research needs via the annual update of the regulatory science research needs list

How to get in touch for comments or to ask questions

If you are an interested researcher or funder, please get in touch if you:

- Have general comments regarding the regulatory science research needs (RSRN) list
- Have comments on a particular topic in the RSRN
- Want to share details of your planned research on a topic in the RSRN or are already working on a topic in the RSRN
- Wish to share relevant research results concerning a topic in the RSRN
- Want to recommend a topic which is not on the current RSRN

For topic-related questions, please click on the link of the respective topics in the list below, which generates a pre-filled email to facilitate contact.

For general questions, please contact us at regulatory.science@ema.europa.eu adding "RSRN" to the subject line of your enquiry.

Continual updating

The RSRN list is a *living* document which will be continually updated with questions by Scientific Committees, Working Parties and subject matter experts across the network based on emerging needs identified in the context of regulatory operations:

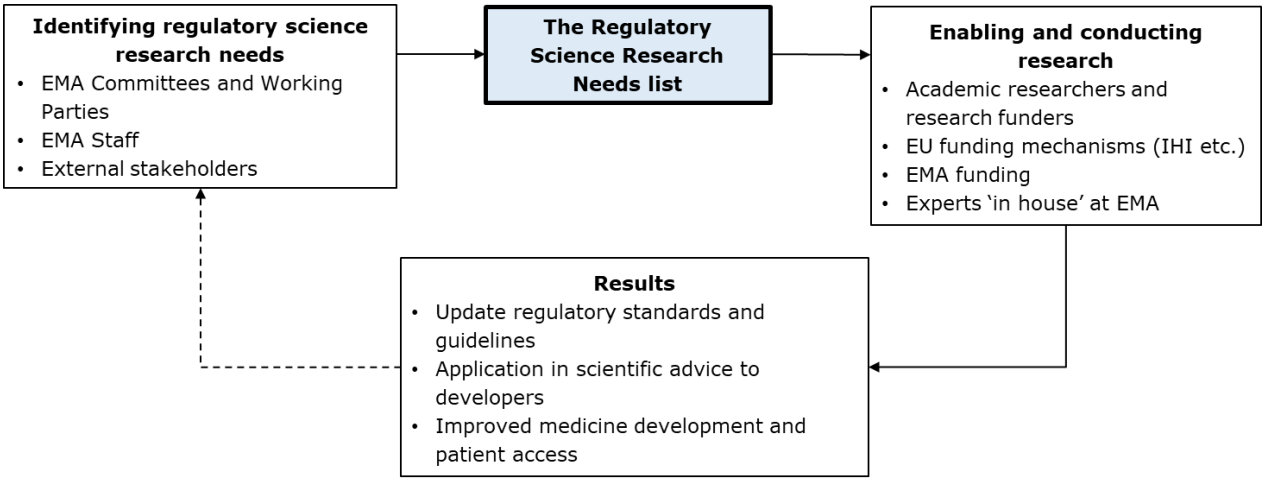

Figure 1. Process map of EMA's Regulatory Science Research Needs list

List of Regulatory Science Research Needs (RSRN)

The RSRN list is structured according to the Regulatory Science Strategy (RSS) Strategic Goals for Human and Veterinary Medicines.[2] This is version 1.0 of the list of Regulatory Science Research Needs.

The column "Research topic" represents the identified needs for the regulatory science research for consideration of researchers and funding organisations to address.

Supplementary information is in the columns "Objectives" and "Expected impact".

Please click on the link in the column "Number" to send an email concerning the particular question.

[1] Research topic concerns human and veterinary medicines.

H1 Catalysing the integration of science and technology in medicines development

Number (click to send email)	Research topic	Objectives	Expected impact
H1.1.1	Establish the best practices and standards for validation of surrogate endpoints and biomarkers for both regulators and HTA/Payers.	To review and describe the evidentiary standards for novel endpoints and biomarkers by EMA and HTA (and potentially payers). To gain an understanding of how standards differ among regulators and HTA/Payers and the evolution of these over time. To evaluate, in collaboration with HTAs, payers and patients, the impact of treatment on clinical outcomes measured by biomarkers, and develop joint standards for biomarker development. To develop guiding principles for surrogate endpoint validation that are acceptable to regulators, HTA and Payers.	Greater clarity in terms of data requirements and facilitating the development of novel endpoints, biomarkers and their qualification. Increased understanding and harmonisation (where appropriate) among stakeholders for novel endpoint and biomarker qualification. Ensuring a shared understanding about the clinical relevance of biomarkers used in developments, and widening their acceptability amongst stakeholders to ultimately facilitate drug development (e.g., improving the speed, cost, objectivity, validity, reliability of clinical trials) with biomarkers used as surrogate endpoints.
H1.1.2	Conduct comprehensive review to identify strong candidates among clinically validated biomarkers for regulatory qualification.	To leverage EU research to identify and further support development of clinically validated biomarkers. To map, understand and qualify the latest clinically validated biomarkers.	Bringing clinically validated biomarkers for qualification, facilitating their use and the improved development of medicines.
H1.2.1	Map the scientific and technical bottlenecks for the alignment of regulatory authorities for multisite manufacturing of ATMPs, including decentralised manufacturing.	To address the challenges of decentralised ATMP manufacturing and delivery locations; To test new approaches of taking ATMP manufacturing to bed side.	Ensure that the decentralised manufacturing of ATMPs is consistent across care centres to ensure the effective and safe use of ATMPs. To provide support to developers seeking to manufacture ATMPs at multiple sites.

Number (click to send email)	Research topic	Objectives	Expected impact
H1.2.2	Explore the organisational and infrastructural needs to improve the translation of ATMPs from clinical development to clinical use (including bed-side manufacturing) in close collaboration with HTAs.	To understand two gaps in decision-making process relating to ATMPs: 1. Delays in access due to unsuccessful reimbursement decisions partly due to high costs, including products initially developed by academia. 2. Knowledge gaps of the regulatory process among academic ATMP developers which hinder early dialogue and collaboration with regulators.	Wider and earlier engagement with academia to bring ATMP researchers into the regulatory system to ensure safety and efficacy of ATMPs. Ultimately enhancing the impact of public investment into ATMP development.
H1.2.3	Conduct research to improve the understanding of funding mechanisms for ATMP development and propose solutions for funders and developers to increase the number of ATMPs and associated methods, devices, companion diagnostics that become available for patients.[1]	To map out the current funding mechanisms for ATMP development in Europe. To understand and analyse the criteria behind granting funding. To provide a regulatory perspective on funding mechanisms for ATMP development in Europe. To increase the regulatory knowledge of academic developers of ATMPs.	Optimised investments into ATMP development, resulting in higher translation into the clinic.
H1.2.4	Review the predictivity of non-clinical data for ATMP development to inform the management of adverse drug reactions and to inform risk management plans of authorised ATMPs, including identification of promising non-clinical methods in particular from EU research projects.	To identify gaps and propose new models in the ATMPs safety testing flow that might be addressed by novel non-clinical models for which EU funded studies have already generated results	Increases efficiency in developing ATMPs and increased knowledge of the safety of these products.
H1.3.1	Analyse the impact of PRIME on clinical development and access to medicines in health care systems.	Measure the impact of PRIME on patient access to medicines.	A quantification of the value that enhanced development support through PRIME provides patients, would allow better-evidenced decisions on regulatory development support.

Number (click to send email)	Research topic	Objectives	Expected impact
H1.4.1	Review novel manufacturing and delivery approaches (including devices) to identify potential regulatory limitations and bottlenecks for the use of these technologies.[1]	Understand and highlight regulatory limitations and bottlenecks for: 1. Digital manufacturing, and AI learning, e.g. process control and automated batch release, Pharma 4.0, also continuous manufacturing 2. Devices. Research into what medicines regulators could learn from novel materials / engineering in devices and their regulation. 3. Digital medicines. Personalised manufacturing and monitoring	1. Efficient and robust manufacturing controls, optimised regulatory oversight. 2. Improve regulatory application of risk-based approaches. 3. Impact on patient compliance and personalised manufacturing technologies
H1.6.1	Develop an understanding of, and regulatory response to, nanotechnology and new materials in pharmaceuticals anticipated to be used in the coming 10 years.[1]	To develop understanding of and regulatory response to nanotechnology and new materials in pharmaceuticals: 1. Conduct Horizon scanning into medicines composed of novel nano materials which may not be amenable to conventional CMC characterization, PK and PD approaches.	A better prepared EMRN for advice and regulation of nanomedicines and MP in combination with medical devices.
H1.6.2	Identify data and/or new methods needed for the adequate chemistry manufacturing controls (CMC) characterization of forthcoming nanotechnologies.[1]	To develop understanding of and regulatory response to nanotechnology and new materials in pharmaceuticals: 1. If needed, conduct research to develop methods and data adequate for regulatory decision making. For example, and investigate PK strategies and PD biomarkers for a given category of generic and innovative nanomaterial (e.g. new polymer mixtures, composite metal core nanoparticles). Establish a collaboration with the EC-JRC laboratories and the IPRP nanomedicines working group on regulatory research in the area.	A better prepared EMRN for advice and regulation of nanomedicines and MP in combination with medical devices.

Number (click to send email)	Research topic	Objectives	Expected impact
H1.7.1	Research on lesson learned and impact analysis from EMA's involvement in EU-funded projects.[1]	1. Evaluate the extent and impact of EMA regulatory interactions with EU-funded projects 2. Identify gaps / opportunities for improvement 3. Recommendations for EMA's interactions with EU-funded projects	Advancing the success of EU-funded projects and/or improving the efficiency of resource allocation, e.g. ensuring that outcomes of EU funded projects are incorporated into medicines regulation
H1.7.2	Explore novel types of regulatory science support for product development, analysing the approaches of other regions and their potential application in the environment of the European Union.	1. Map the regulatory support provided to medicines' developers across global regions 2. Use these, and the stakeholder input received in the Regulatory Science to 2025 to liaise with EMA's scientific committees and develop new and integrated regulatory advice provision. 3. Ensure new advice provision protects against conflicts of interest	1. Better regulatory advice provision 2. Positive impact on patient-centred medicines development in the EU

H2 Driving collaborative evidence generation - improving the scientific quality of evaluations

Number (click to send email)	Research topic	Objectives	Expected impact
H2.1.1	Conduct research to identify the best approaches to stimulate developers to use novel pre-clinical models, including those adhering to the 3Rs.[1]	Review results of 3R research from previous EU funded pre-clinical studies and existing literature. Compare and contrast these studies with those submitted non-clinical data in SA and recently approved files. Define the underutilised 3R approaches and best approach to incentivising their use. Identify obstacles to moving from animal models to non-animal alternatives.	Encourage the use of 3R methods and reduce animal testing in medicines development.

Number (click to send email)	Research topic	Objectives	Expected impact
H2.2.1	Understand and provide solutions to the methodological, organisational and regulatory challenges for complex clinical trials that involve multiple companies and products.	To support the development of treatments in conditions where there are candidates but developmental hurdles. To foster the conduct of clinical trials with adaptive models for multiple candidates for a disease where there is no effective treatment but where there is a solid understanding of the mechanism of action. To foster multi-stakeholder dialogue into the feasibility of umbrella trials.	Potential to bring products to market and foster collaborative business models.
H2.2.2	Undertake research to assess the Estimands Framework of ICH E9(R1) for methods used for indirect comparisons.	To evaluate and improve the methods used for indirect comparisons of treatments in light of the Estimands Framework of ICH E9(R1).	Different trials may consider different estimands or intercurrent events which complicates indirect comparisons between trials. Research on this topic will improve understanding about limitations and improve the quality of indirect comparisons by identifying or developing suitable methods. Evidence of value can inform: - regulators: for example in the context of assessing significant benefit for an orphan designation, - HTAs and payers: to understand which treatments to prioritise, - prescribers: to make informed individual decisions.
H2.2.3	Assess the utility of real-world healthcare data to improve the quality of randomised controlled trial (RCT) simulations.	To improve the quality of RCT simulations by leveraging real-world healthcare data.	Simulations in the context of randomised controlled trials may be used at the trial planning stage or to support the results observed during the trial. Leveraging real-world healthcare data to inform the simulation, might help to improve the quality of the simulations by providing the data needed to refine the assumptions on the data-generating mechanisms, e.g. to calculate power when designing RCTs or for methodological research.

Number (click to send email)	Research topic	Objectives	Expected impact
H2.2.4	Conduct trend analyses of key features of clinical trials with patients with a cancer for marketing authorization, such as location, type, size, methodology etc., and explore trends in relation to activities for and impact of Europe's Beating Cancer plan.	To understand how this important program affects conduct of clinical trials.	Contributes to the understanding of the baseline of cancer clinical research features and of success factors for the conduct and regulatory use of cancer trials, thus informing considerations for the support of trials to be impactful.
H2.4.1	Research how to optimize EMA's assessment report and opinion documents to ensure a wider and simplified benefit-risk communication, in particular for medicines supported with PRO studies.	To review and describe existing guidelines on designing, conducting, analysing and reporting PRO studies and assess the need for further EU regulatory guidance as well as international harmonisation.	Improved understanding among external stakeholders on the key elements underlying the opinion.
H2.4.2	Research how to best communicate evidence uncertainties provided in the EPAR to support HTA decision-making.	To provide additional clarification on the evidence uncertainties listed in the EPAR so that HTA bodies can have a better understanding of them. To support HTA bodies in their decision-making.	Improved transparency and communication towards HTA bodies about the benefit-risk assessment.
H2.4.3	Establish an optimized series of quantitative benefit-risk methodologies to be implemented in the scientific evaluation of marketing authorisation applications.[1]	To explore the feasibility and efficient implementation of quantitative benefit/risk analysis. To define guiding principles for case selection and efficient implementation with a view on enhancing the reusability of these quantitative models between products and stakeholders.	Improved transparency and communication towards external stakeholders about the benefit-risk assessment
H2.5.1	Support the conduct of targeted studies that would advance paediatric and rare disease medicinal product development through characterisation of the natural history of the diseases/conditions, identification of genotypic and phenotypic subpopulations, and development and/or validation of clinical outcome measures and biomarkers.	Promote natural history studies in rare and paediatric diseases that help address high unmet needs. Identify suitable clinical study endpoints for medical development.	Identify suitable clinical study endpoints, relevant to patients as well as regulators in diseases for which we currently know very little and there is a high unmet need.

Number (click to send email)	Research topic	Objectives	Expected impact
H2.5.2	Conduct research to understand the potential effects of medicines on foetal health and pregnant women.	Advance our understanding of interference, and prevention thereof, in foetal programming. Including a focus on the effects of medicines.	Better prediction of reproductive toxicity leading to reduced uncertainty for medicine use in pregnancy & breastfeeding
H2.5.3	Conduct research to analyse the impact of imposed regulatory precautions for high-risk products used in materno-foetal health.	Build on work already in progress: 1) Develop an inventory of existing Pharmacovigilance and Risk Minimisation Measures for this population 2) Evaluate their impact; 2.1) Evaluate discrepancies between implementation in different member states; 2.2) Identify where (if anywhere) need for harmonisation across products / across member states is required; 2.3) Evaluate whether there is room for improvement and if so, develop strategies for achieving such improvement	1) Better informed medicine use in pregnancy and breastfeeding i.e. importantly reduced uncertainty, ideally leading to 2) enhanced B/R of medicine use in pregnancy and breastfeeding and 3) a healthier population
H2.5.4	Identify areas of highest unmet needs where real-world evidence (RWE) can supplement clinical trial data in regulatory decision-making. Investigate corresponding methodological approaches.	To define the most promising special populations and data for which RWE can be utilised to supplement RCT data and enhance regulatory decision-making. Define the sources of data and methods for using such RWE.	Enhanced regulatory decision making for special populations.
H2.5.5	Conduct research to understand determinants for the implementation of physical frailty assessment tools as per the CHMP "Reflection paper on physical frailty: instruments for baseline characterization of older populations in clinical trials" (EMA/CHMP/778709/2015).	To describe key factors in frailty assessment in elderly. To understand how those factors affect frailty assessment.	To better utilize physical frailty assessment tools in clinical trials.

Number (click to send email)	Research topic	Objectives	Expected impact
H2.5.6	Conduct research and develop methods for predicting, detecting and assessing signals of suspected adverse reactions and risk factors for susceptibility to adverse reactions in special populations, taking into account functional status, concurrent diseases and medication, age-related physiological changes or medicines' use aspects.	1) Develop innovative and more efficient methods for detecting and assessing adverse reactions in patients with multiple risk factors. Consider data analytics to develop methods and explore whether extrapolation of safety data from younger adults be used. 2) Use these methods to support the benefit/risk evaluations and decisions on risk minimisation measures, including safe use advice. This should take into account concurrent medical conditions of high prevalence in the older population, such as diabetes and cardiovascular diseases.	Protect susceptible populations from adverse reactions in clinical trials. Better determination of the benefit / risk relationship in complex populations. Improved risk minimisation measures aiming at reducing patient harm
H2.5.7	Design new toxicology studies for special populations, after reviewing data already available for new toxicology models (organoids and foetal stem cells systems) in foetal, young and old animals.	To address the need for toxicology studies to better inform the use and safety assessment of medicines in special human populations	Better inform clinical trials and medicines use
H2.5.8	Conduct research to facilitate the implementation and uptake of recommendations in the "Reflection paper on the pharmaceutical development of medicines for use in the older population" (EMA/CHMP/ QWP/292439/2017).	To understand key determinants when developing medicines for elderly.	Improve the efficiency and scientific quality of drug developments for the older population.
H2.6.1	Conduct research to advance understanding the operating characteristics of Bayesian methods that borrow information on the treatment effect.	To develop standards on the regulatory acceptability of Bayesian methods that borrow information on the treatment effect.	Paediatric extrapolation is an area where techniques such as Bayesian statistics can be used to generate relevant data to support regulatory decision making. Currently, regulatory acceptability of proposed methods is mostly decided on a case-by-case basis, requiring the applicant to provide extensive simulations. The development of standards would reduce the burden on applicants and regulatory assessors.

Number (click to send email)	Research topic	Objectives	Expected impact
H2.7.1	Explore the use of natural language processing (NLP) to structure and analyse unstructured text such as in real-world data (RWD).	Explore the use of natural language processing to structure and analyse unstructured text data.	Robust and trustworthy text mining tools allow the harvesting of relevant information in unstructured text data in RWD, which cannot be effectively handled manually, such as mining medical notes for diseases. Identifying which models perform best under which scenarios will facilitate the choice of data extraction method and knowing their performance will also increase trust in the use of NLP methods as decision support systems in the drug regulatory environment.
H2.7.2	Develop annotated corpora and pre-trained language models for use in biomedical natural language processing applied to real-world text data sources that outperform models pre-trained on general purpose text, that are scalable and that are multilingual in the official EU languages.	Development of tools that identify and extract information from unstructured text data, and facilitate the development and deployment of statistical NLP methods. These tools should lead to more efficient regulatory processes.	The use of scalable pre-trained models will speed-up the development of tools to identify and extract information from unstructured text data, and facilitate the development and deployment of statistical NLP methods. Current pre-trained models use general purpose text (e.g. product reviews, Wikipedia), by using a model specific for biomedical language across multiple languages, the ability to extract relevant information from unstructured fields in RWD from any source in the EU is increased, resulting in more data, and of better quality than that achieved by using general models.
H2.7.3	Explore the use of natural language processing and machine learning techniques to enhance the efficiency of literature screening activities for regulatory purposes.	Explore what natural language processing and machine learning techniques could be used for literature screening. Compare their efficiency and applicability to literature screening in a regulatory context.	Natural language processing and machine learning techniques may support efficiency of literature screening activities by reducing the manual workload.

Number (click to send email)	Research topic	Objectives	Expected impact
H2.7.4	Investigate the use of machine learning models in estimating heterogeneity of treatment effects.	Investigate the use of machine learning models in estimating heterogeneity of treatment effects.	Heterogeneous treatment effect techniques help identify subsets of a population that have better or worse outcomes on a medicinal product. This research will provide a deeper insight on individual patient data beyond the traditional average treatment effects and help identify unmet medical needs.
H2.7.5	Test the ability of machine learning methods to help identify relevant healthcare data to match with and interpret single-arm trials and randomised controlled clinical trials augmented with real-world data (RWD).	To deepen understanding about the ability of machine learning methods to help identify relevant healthcare data to match with and interpret single-arm trials and randomised controlled clinical trials augmented with RWD.	Manual search for relevant healthcare data supporting the contextualisation of single-arm trials or the augmentation of randomised clinical trials is time consuming. Machine learning methods may help to expedite the search by identifying suitable healthcare data. To generate an efficient system to identify datasets that can be used to contextualise the evaluation of new medicines in the EU, supporting the conduct of clinical trials.
H2.7.6	Assess if and how machine learning methods can be systematically harnessed to screen a large amount of data in many electronic databases to identify factors affecting efficacy and safety of treatments.	To deepen understanding about how machine learning methods can be systematically harnessed to screen a large amount of data in many electronic databases to identify factors affecting efficacy and safety of treatments.	Establish a learning health care system with a strong public drive to increase the value of health care data beyond their traditional use for testing specific hypotheses by developing methods for the monitoring of the safety and effectiveness of medicines and for signal detection.
H2.7.7	Identify and define regulatory requirements to validate AI algorithms used in the context of regulated medicines.	Develop a framework to validate Artificial Intelligence (AI) algorithms used in the context of regulated medicines and define their regulatory acceptability.	Establishing a framework for the validation of AI algorithms will ensure a harmonised assessment approach for the acceptability of AI algorithms in the context of regulatory decision making.
H2.7.8	Promote the development of global principles around the use of AI based technology in healthcare related fields.	Develop global principles around the use of AI based technology in healthcare related fields.	Ensure the definition of global principles (e.g. related to ethics, use cases, methods) around the use of Artificial Intelligence based technology in healthcare related fields.

H3 Advancing patient-centred access to medicines in partnership with healthcare systems

Number (click to send email)	Research topic	Objectives	Expected impact
H3.1.1	Conduct research to optimally interface early access regulatory tools and process (e.g. conditional marketing authorisation) into decision-making by HTAs and payers on access for patients.	Define what elements of early access regulatory tools and processes challenge HTA and Payer decision-making. Work with these stakeholders to address these challenges and better interface early access decision-making.	Earlier access to safe and effective medicines
H3.1.2	Explore if and which methods such as multi-criteria decision analysis can be used across regulatory, HTA and Payers' decision-making.	To explore the usefulness of a common methodology for the common aspects of decision-making by regulators (benefit-risk), HTAs (relative effectiveness) and Payers (value-cost) to facilitate inter-operability, communication on these assessments, and transparency on the different decisions.	Clarifying the European regulatory landscape and requirements. Advancing understanding of decision-making and highlighting cases which may allow common approaches between decision-makers. Improving transparency of decisions and facilitating drug development and access.
H3.3.1	Conduct research to optimize medicinal products' efficacy and safety in patients in specific therapeutic areas, such as oncology, from early development to post-authorisation use in real-world settings.	To explore how the Agency can help to address the evidence gaps that remain after medicines have been approved. To evaluate whether the uncertainties that payers and clinicians are faced with regarding new medicines can be identified prospectively and tackled early on in medicines development.	An improved understanding of how medicines should be used in clinical practice, leading to fewer uncertainties about their effects, better outcomes for patients and a more efficient use of healthcare resources
H3.3.2	Develop standards for patient-reported outcomes (PROs) to be used to assess the utilities of treatments in order to inform regulatory and potentially HTA decisions.	To work with HTAs to assess the feasibility of identifying and/or qualifying a core health-related quality-of-life PRO to implement in trials and to bridge the gap with comparative effectiveness assessment. To establish guiding principles on sufficient evidence to consider PRO instruments as "validated" and develop an inventory of validated PROs To review and describe existing guidelines on designing, conducting, analysing and reporting PRO studies and assess the need for further EU regulatory guidance as well as international harmonisation.	Greater clarity in terms of quality requirements for PRO studies and better evidence generation for benefit-risk assessment and HTA in oncology and other therapeutic areas

Number (click to send email)	Research topic	Objectives	Expected impact
H3.3.3	Conduct research to understand the optimal approaches for patient input into the benefit-risk assessment in decision making.	To optimise patient impact into regulatory assessment. To identify optimal approaches for patient preferences elicitation that are feasible in a regulatory context. To gather evidence on the efficacy and most effective ways of patient consultation and preference elicitation.	Enhancing patient involvement and therefore the regulatory process in Europe
H3.3.4	Conduct research to understand and develop standards to incorporate patient preferences in the assessment of utilities of treatments to inform regulatory and potentially HTA decisions.	To assess through case studies and simulations the usefulness of estimating individual patient utilities based on individual outcomes and preferences for making benefit-risk decisions and relative effectiveness decisions, respectively. To review and describe (methodological) guidelines/recommendations regarding patient preference studies (e.g. ISPOR, PREFER, regulatory agencies). To identify best practice patient preference studies and characterise their strengths and weaknesses. To develop preliminary guiding principles for the conduct of patient preference studies aiming to inform decisions by regulatory agencies and potentially HTA/payers.	Developing methods on how to enrich the benefit-risk assessment and decision-making with patient utilities. Highlighting where endpoints are not translating into patient benefit, or where clinical benefit also comes at a cost to the patient. Developing guiding principles for using such approaches. Greater clarity in terms of quality requirements for patient preference studies.
H3.3.5	Review methodologies to be used to systematically gather and use patient data from the wider patient community during medicines' benefit-risk evaluation.	To review and describe (methodological) guidelines/recommendations regarding patient preference studies (e.g. ISPOR, PREFER, regulatory agencies). To identify best practice patient preference studies and characterise their strengths and weaknesses To develop preliminary guiding principles for the conduct of patient preference studies aiming to inform decisions by regulatory agencies and potentially HTA/payers	Increased understanding on how to better align benefit-risk assessment with patient values and preferences

Number (click to send email)	Research topic	Objectives	Expected impact
H3.3.6	Develop the standards and quality requirements for designing, conducting, analysing and reporting PRO studies for regulatory submission and to understand how these quality requirements help evaluating the evidence from PRO studies during benefit-risk assessment.	To contribute to systematically incorporate patient-reported outcomes into medicine development and the evaluation of benefits, harms and uncertainties.	Greater clarity in terms of quality requirements for PRO studies and better evidence generation for benefit-risk assessment and HTA.
H3.3.7	Develop the standards on quality requirements for designing, conducting, analysing and reporting patient preference studies for regulatory submission and to understand how these quality requirements help evaluating the evidence from patient preference studies during benefit-risk assessment in key therapeutic areas such as oncology.	Collect patient preferences regarding the benefits and risks of oncology drugs using a stated preference method based on value theory/utility theory (e.g. swing weighting or discrete choice experiment). Identify and describe preference heterogeneity according to patient (cultural, demographic, clinical, psychological) characteristics. Establish a database containing the obtained results of the study, namely patient-level data including their characteristics and stated preferences. This database will allow to conduct further analyses to characterise patient preferences, explore any characteristics associated with different preference profile and inform the benefit-risk of oncology drugs.	Greater clarity in terms of quality requirements for patient preference studies in different therapeutic areas.
H3.4.1	Research into methods, feasibility and reliability for using social media data for detecting adverse events including under circumstances such as potential abuse, clinical errors, multiple medications, prescribing mistakes.[1]	To explore if and how use can be made of new digital technologies and communication channels (such as social media) to provide added value for the monitoring of medicines, in particular their safety.	Relevant improvement of the monitoring of medicines, including for their safety.

Number (click to send email)	Research topic	Objectives	Expected impact
H3.4.2	What are important evidentiary standards for the use of real-world evidence (RWE) for regulatory scientific advice and decision-making on the safety and efficacy / effectiveness of medicines?[1]	Develop a set of evidentiary standards to be pre-specified and used in the analysis of real-word evidence applied to different types of regulatory advice and decisions on the safety and efficacy / effectiveness of medicines (e.g. in complement to clinical trial data in an authorisation application, or for extension of indications, amendment to product information or regulatory actions on the marketing authorisation due to safety concerns).	Developing standards will support patient access to safe and effective medicines by facilitating consistent and valid evidence-based decisions in the absence of clinical trial data or when clinical data need to be supplemented with real-world evidence.
H3.4.3	Deepen the understanding of the role of real-world data (RWD) in providing evidence to support marketing authorisation applications.	Establish methods and processes to enable continuous learning from pre-authorisation procedures and authorisation applications to medicines regulators that contain RWD.	Ensuring that the outcome of use of RWD in the development and supervision of medicines is known will enable regulators, pharmaceutical companies, HTA bodies and payers to learn from experience and, over time, to make better decisions when advising on studies to be performed and on assessing and interpreting the results of those studies.
H3.4.4	Promote the development of standardised processes and methods for accessing real-world data (RWD) in order to support the performance and efficiency of large randomised clinical trials.	Enhance the performance and efficiency of large randomised clinical trials by developing standardised processes and methods to access RWD, including electronic health care record systems, specialised registries and hospital databases.	This will support patient access to innovative therapies by facilitating the performance of larger, cheaper and faster randomised clinical trials. It will further support the evaluation of the value of new medicines by health technology assessment bodies.
H3.4.5	Identify and define important methodological standards for the regulatory acceptability of real-world data (RWD) in the context of single-arm and randomised controlled clinical trials augmented with RWD.	To define methodological standards for the regulatory acceptability of real-world data (e.g. from electronic health care records, disease registries, other data sources) in the context of single arm trials and randomised clinical trials augmented with real-world data (e.g. supporting unequal randomisation ratio with fewer control subjects).	This will contribute towards rapid patient access to new medicines for rare diseases by supporting regulatory decision-making based on small trial populations.

Number (click to send email)	Research topic	Objectives	Expected impact
H3.4.6	Identify and scrutinise case scenarios on how real-world evidence (RWE) complements RTCs establishing efficacy and safety of medicines, so as to develop a methodological framework for a consistent application of relevant methodologies.	To establish case scenarios to understand the complementary roles of RWE and RCTs. To develop methodology framework to guide future application.	Consistent application of valid and robust methodology.
H3.5.1	Promote the development of a common data quality framework across different types of real-world data (RWD) sources.	To contribute to the development of a standard data quality framework reproducible across different types of real-world data sources, with a characterisation of the data collection, management and reporting and an empirical data quality validation.	Transparency and demonstration of data quality will increase confidence in the validity of the study results and their interpretation.
H3.5.2	To develop a framework for the management, analysis and interpretation of heterogeneity in observational studies using different databases	To develop and test methods for: 1) identification of different types of heterogeneity (incl. possible differences across different outcomes) and metrics for their measurement; 2) prediction of heterogeneity through cohort diagnostics, analytical diagnostics, summary scores; 3) minimisation of unwanted heterogeneity at study design (e.g. through use of negative controls); 4) visualisation and documentation of heterogeneous results; 5) analytic techniques, including consideration to small cell counts and appropriate use of meta-analysis; 6) interpretation and reporting.	To support use of multi-database studies providing real-word evidence (RWE) on large and diverse populations, thereby increasing representative-ness and precision of the evidence for regulatory decision-making.

Number (click to send email)	Research topic	Objectives	Expected impact
H3.5.3	Leveraging available information on medicines prescribed, sold or administered, in electronic databases at different levels of the health care system.	Develop methods for the integration of available information on medicines prescribed, sold or administered in electronic databases at different levels of the health care system.	Creating a representative and comprehensive database of exposure to medicines where medicinal products are administered at different levels of the health care system and where the information is disparate across the health care system will improve access to relevant information for determining the medicines benefit-risk profile (e.g. for the administration of vaccines in a mass vaccination campaign).
H3.6.1	Investigate options to make the EU Package Leaflet more user-friendly and investigate how effective such changes are.[1]	To identify, in consultation with stakeholders, specific areas where improvements are needed to the EU PL and associated guidelines, in particular to improve readability, design and layout. To test whether the proposed changes increase understanding of the PL, medication adherence and health literacy.	Clearer guidance and improved readability of the PL will increase patient understanding and should contribute to patient safety, treatment compliance and overall a more rational use of medicines.
H3.6.2	Conduct research to identify the best practices to use the EU-wide harmonised electronic patient information (ePI) in EU Member states.	To ensure an optimal use of ePI by patient and healthcare professional groups, and ensure optimal integration into eHealth in the different Member States	Improved patient well being and quality of care and positive contribution to sustainable health systems. Provision to patients / consumers and healthcare professionals of needed information from the PI at various points in the treatment journey, including information on use and administration of the medicine, how to recognise possible side effects and how to act in the light of new safety data.
H3.6.3	Establish a systematic methodology framework to monitor and evaluate the usefulness of the EU-wide electronic patient information (ePI) system for its target user groups.	To measure how and if access to digital product information translates into improved patient safety and better health outcomes. To measure how improved health information can support effective risk minimisation. To establish the proposed baseline, targets and metrics to measure such impact.	Established methodology, agreed with stakeholders and interested parties, to monitor and measure impact and effectiveness of electronic health information systems, including ePI.

Number (click to send email)	Research topic	Objectives	Expected impact
H3.7.1	Promote research to identify key knowledge gaps between stakeholders to improve existing information materials on biosimilars to improve update and acceptance.	1. Identify knowledge gaps among patients, healthcare professionals and payers that hamper the optimal use of biosimilars in healthcare systems. 2. Assessment of effectiveness of available information materials with a view to implement further improvements.	To ensure optimal uptake of biosimilars in the healthcare systems and avoid misconceptions.
H3.7.2	Address regulatory challenges in manufacturing e.g., statistical assessment of critical quality attributes (CQAs) in the comparability exercise and the evolution of multisource biologicals/biosimilars.	1. Further the academic development of sensitive analytical technologies for the purpose of comparability, e.g. NMR, functional assays. 2. Statistical methodology in comparability assessments: increase regulatory understanding of use of different statistical approaches and how these could be used to improve robustness of regulatory decision making. 3. International convergence: identify divergencies between regulators that serve as bottlenecks for global development of biosimilars.	Improve regulatory decision making and reduce the need for unnecessary non-clinical and clinical studies. Further global convergence in the area of biosimilars.

H4 Addressing emerging health threats and availability/therapeutic challenges

Number (click to send email)	Research topic	Objectives	Expected impact
H4.1.1	Proactively identify areas of public concern to improve evidence-based information on emerging health threats, including pandemic vaccines.	To identify by gap analysis areas where scientific evidence is missing or should be improved and drive research accordingly. To explore optimal mechanisms and methodology to facilitate timely integration of research output into the scientific regulatory assessment. To engage in continuous dialogue with patients, consumers, healthcare professionals and academics to monitor and respond promptly to societal concerns on medicines for emerging health threats such as pandemic vaccines.	Increased preparedness for timely and effective communication and engagement with the public in emerging health crisis. Increased public trust and transparency. Established and continuous mechanism to monitor efficacy of interventions and to promptly identify new concerns.
H4.1.2	Conduct research into lessons learned from COVID-19 for the optimisation of scientific and regulatory pathways for new treatments for emerging pathogens.	Develop the science and pathways for the advancement and approval of vaccines and therapeutics ahead of epidemics. Define processes that allow rapid manufacturing and testing during an emergency. Formalise more systematic interactions with developers of novel therapeutics/ vaccines.	High impact on continuous outbreaks with emerging pathogens and the need for as rapid response as possible. Platform technologies might be easier to scale up and transfer to different manufacturing sites and require regulatory support.
H4.1.3	Evaluate how to improve operational preparedness for future crisis, integrating also the new, extended mandate for EMA.	Learning lessons from COVID-19, implement best-practice crisis planning across the EMA to ensure maximal preparedness for future health threats.	Effective response in the context of health emergencies
H4.2.1	Conduct research to support alternative approaches to new antibacterial drug development and innovative approaches for the prevention and treatment of infections.[1]	For such developments, to optimise evidence gathering, the use of PK/PD should be exploited. Training for the EMRN should be developed to this end. Refine endpoints for serious infections, e.g. HAP/VAP. Support the establishment of clinical trials networks for such developments. Re-establish international dialogue and dialogue on alternatives to traditional antibiotics.	Rapid development of new antibacterial agents in areas of unmet need related to AMR

Number (click to send email)	Research topic	Objectives	Expected impact
H4.2.2	Conduct research to define evidence requirements for new antibacterial medicines that are acceptable for regulators, HTA and Payers.	Encourage development plans for antimicrobials that are sufficient for HTA and payers. Support initiatives from HTAs/payers that attempt to redefine the criteria for added value for new antibacterial agents.	Positive perception towards the evidence needs of developers and thereby stimulating developers to come forward with proposals.
H4.2.3	Improve the understanding and usefulness of regulatory support to the development and application of rapid diagnostics tools (RDTs) to avoid empirical anti-microbial treatment.[1]	Promote the use of rapid diagnostics tools (RDT) in clinical trials as companion diagnostics or even co-development as the best tool to ensure rational use and avoid over-treatment.	Considerable impact on rational and personalised use of new antibacterial agents, some of which are active on single species and require the availability of RDT.
H4.3.1	Conduct research in support of international harmonisation of regulatory science standards for complex generic medicines addressing bioequivalence, waivers and modelling.	To generate data to support regulatory decision making on generic medicines throughout the product life-cycle. Currently there may be gaps in knowledge when it comes to approving (complex) generic medicines. The necessary questions cannot be put to the innovator companies and some generic companies may lack the resources and expertise to address the issues. This means decisions may be driven by expert opinion in the absence of data. Closing this knowledge gap could result in more definitive regulatory positions e.g. product specific guidelines for bioequivalence for generics 1. Research questions coming out of international initiatives e.g. IPRP 2. Look at the models of bioequivalence and how these can lead to more robust data / approval - use liposomal doxorubicin as example).	The impact would be access to cheaper and safer generic medicines bearing in mind that up to 80% of prescriptions are for generics. There is also a potential impact on switchability between products which although handled at national level in the EU, would benefit from data-driven centralised positions on the underlying scientific concerns.

Number (click to send email)	Research topic	Objectives	Expected impact
H4.4.1	Investigate and identify communication strategies to improve evidence-based information to foster trust and confidence in vaccines.	Drive research to improve and optimise the use of existing tools and methodology to better communicate benefit-risk of vaccines. Further research is needed to optimise handling of scientific uncertainty, focusing on how to best address and communicate it.	High quality and understandable information on quality, benefits and risks of vaccines is the basis for many other interventions at national, EU and globally to foster vaccine confidence.
H4.4.2	Conduct research into approaches that strengthen data analytics including data visualisation by regulators for pharmacovigilance and risk communication, in particular during a pandemic and for vaccine supervision.	To improve the use of data analytics in pharmacovigilance. To define the optimal tools for risk communication and data visualization from regulators during a pandemic.	Improved use of data analytics and targeted visualisations on benefit risk will strengthen public confidence in regulators during a future pandemic and result in improved medicine uptake.
H4.4.3	Research into improving and leveraging improved clinical trial methodologies and clinical development strategies for vaccines.	Strengthen translational science for more rational and efficient vaccine development. Facilitate conduct of late stage clinical studies.	Efficient dose and schedule selection to facilitate clinical development.
H4.4.4	Research to improve and sustain the operational aspects of the EMA-ECDC platform for generating data for EU benefit-risk monitoring of vaccines after marketing authorisation.	Sustain and improve the platform for the conduct, in the EU, of post-approval effectiveness and safety studies for vaccines. This entails adequate governance for transparent interaction between private and public sector. Mechanisms for funding of studies that address public health authorities concerns should also be defined.	Ability to rapidly address research questions on vaccines B/R and reassure EU citizens on the impact of vaccination programmes.

Number (click to send email)	Research topic	Objectives	Expected impact
H4.5.1	Explore the pooling of data from various data sources in the context of drug repurposing, i.e. to which extent and how can pooled data be used to support a new indication?	To understand the methodology/ principles to enable data-sharing/ pooling from different data sources for repurposing activities (e.g. targeting a new indication). To understand the limitations and use cases of data-pooling, i.e. which scientific questions can exactly be answered by using pooled data.	There is a wealth of data not only from clinical trials but also from academic studies and real-world data which offer the opportunity to identify new indications for currently authorised drugs. The advantages are clear not only in terms of speed of development but also the fact that there is a known safety profile. The combination of regulatory data (marketing authorisation data, variations, periodic safety update reports and EudraVigilance data), real-world data, clinical healthcare data, basic research data and publications could offer new relevant insights. Repurposing of drugs may help to address unmet medical needs and cut development requirements and costs for old products with limited business interest.

H5 Enabling and leveraging research and innovation in regulatory science

Number (click to send email)	Research topic	Objectives	Expected impact
H5.4.1	Develop regulatory training modules for regulatory assessors, including describing innovation of new medicines and their progression from laboratory to patient (wherever possible in collaboration with other research topics in this list)[1]	1. Identify gaps in training for regulators (done by EU-NTC already); 2. Together with EU-IN and EU-NTC draw up a list of learning objectives, key skills & competencies, knowledge & understanding to be achieved through formal courses, 3. Identify potential academic institutions that could provide courses to fill those gaps. 4. Work with those institutions, HMA and EU-IN to develop and deliver those modules.	Improved expertise of the network to provide advice and regulate more effectively and efficiently.

Number (click to send email)	Research topic	Objectives	Expected impact
H5.4.2	Research into unbiased and far-looking horizon scanning methodologies for key areas of innovation in biomedical fields.	1. Establish sustainable Horizon scanning. 2. Publish results 3. Implement the recommendations to ensure preparedness.	A clear grasp of the changes the agency will need to make over a 5-10 year perspective. Allowing a more proactive, strategic Agency.

V1 Catalysing the integration of science and technology in medicines development

Number (click to send email)	Research topic	Objectives	Expected impact
V1.1.1	Research into developing standards for/validating owner-reported assessments/outcomes used to assess efficacy.	Review the novel therapies and new endpoints that are expected to arise over the coming years and analyse any gaps in guidance and standards. This should facilitate the authorisation of novel therapies, helping the Agency to become a centre of excellence.	Facilitation of the authorisation of innovative Marketing Authorisations that could be of benefit for public and animal health as well as for animal welfare, making the Agency a reference regulatory body for innovative veterinary medicinal products.
V1.1.2	Conduct research to improve the understanding of funding mechanisms for innovative veterinary medicine development and work with funders and developers to increase the number of innovative veterinary medicines and associated methods, devices, companion diagnostics that become available.[1]	To map out the current funding mechanisms for innovative veterinary medicines development in Europe. To understand and analyse the criteria behind granting funding. To provide a regulatory perspective on funding mechanisms for innovative veterinary medicines development in Europe. To increase the regulatory knowledge of academic developers of innovative veterinary medicines.	Optimised investments into innovative veterinary medicines development, resulting in higher translation into the clinic.
V1.1.3	Research on lesson learned and impact analysis from EMA's involvement in EU-funded projects.[1]	1. evaluate the extent and impact of EMA regulatory interaction with EU projects; 2. identify gaps / opportunities for improvement; 3. amend our interaction with EU funded projects accordingly.	Advancing the success of EU funded project and/or improving the efficiency of resource allocation

Number (click to send email)	Research topic	Objectives	Expected impact
V1.2.1	Identifying the obstacles to moving from animal models to non-animal alternatives.	1. Reduce the number of experimental animals used. 2. Gain efficiency in regulatory testing and thus VMP marketing authorization processes	Decrease of the number of experimental animals used, increase of consistency of data, reduction of time and costs spent on VMP development and marketing authorisation processes, facilitation of market access for SMEs, increase of availability of new VMPs, improvement of the public perception of (veterinary) medicinal product authorisation.
V1.2.2	Conduct research to identify the best approaches to stimulate developers to use novel pre-clinical models, including those adhering to the 3Rs.[1]	Review results of 3R research from previous EU funded pre-clinical studies and existing literature. Compare and contrast these studies with those submitted non-clinical data in SA and recently approved files. Define the underutilised 3R approaches and best approach to incentivising their use. Identify obstacles to moving from animal models to non-animal alternatives.	Wider use of 3R methods and reduced animal testing in medicines development.
V1.3.1	Elucidate the regulatory bottlenecks faced by novel manufacturing approaches for veterinary medicinal products and how relevant regulations could be modernised.	To ascertain the novel manufacturing methods expected over the coming 10 years and their regulatory bottlenecks. This should facilitate the development and regulatory framework for the use of new technologies and novel approaches to manufacturing of veterinary products (e.g. platform technologies, antigen master files or innovative products).	New technologies will be used in the development of novel therapies which will facilitate the availability of alternative products to antibiotics, novel vaccines to deal with emerging threats in a more efficient manner and the overall availability of veterinary products.

Number (click to send email)	Research topic	Objectives	Expected impact
V1.3.2	Review novel manufacturing and delivery approaches (including devices) to identify potential regulatory limitations and bottlenecks for the use of these technologies.[1]	Understand and highlight regulatory limitations and bottlenecks for: 1. Digital manufacturing, and AI learning, e.g. process control and automated batch release, Pharma 4.0, also continuous manufacturing 2. Devices. Research into what medicines regulators could learn from novel materials / engineering in devices and their regulation. 3. Digital medicines, Personalised manufacturing and monitoring.	1. Efficient and robust manufacturing controls, optimised regulatory oversight. 2. Improve regulatory application of risk-based approaches. 3. Impact on personalised manufacturing technologies.
V1.3.3	Develop an understanding of, and regulatory response to, nanotechnology and new materials in pharmaceuticals anticipated to be used in the coming 10 years.[1]	To develop understanding of and regulatory response to nanotechnology and new materials in pharmaceuticals: 1. Conduct Horizon scanning into medicines composed of novel nanomaterials which may not be amenable to conventional CMC characterization, PK and PD approaches.	A better prepared EMRN for advice and regulation of nanomedicines and MP in combination with medical devices.
V1.3.4	Identify data and/or new methods needed for the adequate chemistry manufacturing controls (CMC) characterization of forthcoming nanotechnologies.[1]	To develop understanding of and regulatory response to nanotechnology and new materials in pharmaceuticals: 1. If needed, conduct research to develop methods and data adequate for regulatory decision making (not only in pharmaceuticals). For example, investigate PK strategies and PD biomarkers for a given category of generic and innovative nanomaterial (e.g. new polymer mixtures, composite metal core nanoparticles). Establish a collaboration with the EC-JRC laboratories and the IPRP nanomedicines working group on regulatory research in the area.	A better prepared EMRN for advice and regulation of nanomedicines and MP in combination with medical devices.

V2 Driving collaborative evidence generation - improving the scientific quality of evaluations

Number (click to send email)	Research topic	Objectives	Expected impact
V2.1.1	Develop models and methodology for the assessment of environmental exposure following use of ectoparasiticides (APE) in pets.	To contribute to more comprehensive knowledge of the risks posed by these products for the environment.	Elaboration of graduated and detailed risk minimisation measures for APE products for pets.
V2.1.2	Contribute to the generation of Environmental Risk Assessment data for 'old' marketed substances for which no data are yet available (through generic procedures for instance).	Explore what previously generated data can be used to fill data gaps on ERA for old substances, to enable their continued, safe use.	New data may be integrated into new approaches in the conduct of ERA.
V2.1.3	Evaluate what role the environment has on the spread of antimicrobial resistance (AMR).	Investigate the role of the environment on the spread of AMR in the environment and transfer of AMR bacteria between animals/humans.	It may improve understanding of benefit/risk balance of VMPs, as well as dossier data requirements at the time of the authorisation.
V2.1.4	Conduct gap analyses of Environmental Risk Assessment (ERA) for innovative products and propose new models to update ERAs; for example, addressing water pollution effects of innovative products.	Evaluate the need to develop a methodology for the environmental safety of innovative products.	Difficult to foresee until an initial assessment is done.
V2.1.5	Assess whether treatment modalities such as nanomedicines and contrast agents require specific Environmental Risk Assessments (ERAs).	To evaluate if certain treatment modalities require specific considerations for ERA; For example: - For nanomedicines, does the physical form of the product influence ERA; - For contrast agents where very large volumes of product used (> 100 mL).	Difficult to foresee until an initial assessment is done.
V2.1.6	Develop additional guidance/models for the environmental risk assessment (ERA) of human medicinal product substances with specific modes of action e.g. cytotoxic, CNS-active compounds using a tailored approach to ERA.	Evaluate the need to develop specific testing paradigms for drugs with specific modes of action e.g. cytotoxic agents and some CNS-active substances. There is concern that psychoactive drugs present in the aquatic environment could adversely affect the behaviour and populations of fish, and other organisms and standard testing does not address these concerns.	High. It could impact categorisation of compounds for which the action limit may not be applicable and inform the next revision of human ERA guideline. Tailored assessments for certain compound categories.

Number (click to send email)	Research topic	Objectives	Expected impact
V2.2.1	Increase capability in modelling, simulation and extrapolation with applications in toxicological assessment, environmental fate and residue depletion.	1. Reduction of the number of experimental animals used. 2. Gain of efficiency in regulatory testing and thus VMP marketing authorization processes.	Decrease of the number of experimental animals used, increase of consistency of data, reduction of time and costs spent on VMP development and marketing authorisation processes, facilitation of market access for SMEs, increase of availability of new VMPs, improvement of the public perception of (veterinary) medicinal product authorisation.
V2.3.1	Research on the relationship between the sales data, the type of veterinary medicinal products and species to the overall adverse event data in EudraVigilance to establish baseline data and identify potential sources of bias.	To improve/refine methodology – develop and improve signal detection methodology. To identify potential sources of bias and underreporting.	Improved scientific rigour of regulatory decisions.
V2.3.2	Develop methodology using new technology, such as mobile phone apps, to increase reporting rates of adverse events for veterinary medicinal products.	Facilitate reporting of adverse events and veterinary medicines by providing timesaving and convenient solutions.	Improved reporting of veterinary adverse events would ensure better oversight of the benefit/risk of medicinal products post-approval.
V2.4.1	Develop communication tools for EMA to improve communication on key issues, such as product issues raising undue alarm.	To utilise best practices in science communication to provide accurate and timely information on key issues to the relevant target audiences via effective and efficient communication strategies. To make the Package Leaflet more user-friendly and investigate how effective such changes are (including use of electronic product information as provided for in 2019/6). To strengthen EMA's reputation as a trustworthy, independent, authoritative, and transparent Agency. To position EMA as the go-to-source of information on VMPs.	High reputational impact. Medium- & long-term Agency impact

Number (click to send email)	Research topic	Objectives	Expected impact
V2.4.2	Research how to best inform the public of the scientific underpinning of new technologies approved, such as biological products including DNA vaccines or gene therapy veterinary medicinal products.	To improve scientific communication activities targeting EU citizens, particularly with regard to novel technologies.	High reputational impact Medium- & long-term educational impact.
V2.4.3	Establish an optimized series of quantitative benefit-risk methodologies to be implemented in the scientific evaluation of marketing authorisation applications.[1]	To explore the feasibility and efficient implementation of quantitative benefit/risk analysis. To define guiding principles for case selection and efficient implementation with a view on enhancing the reusability of these quantitative models between products and stakeholders.	Improved transparency and communication towards external stakeholders about the benefit-risk assessment.
V2.4.4	Investigate options to make the EU Package Leaflet more user-friendly and investigate how effective such changes are.[1]	To identify, in consultation with stakeholders, specific areas where improvements are needed to the EU PL and associated guidelines, in particular to improve readability, design and layout. To test whether the proposed changes increase understanding of the PL, medication adherence and health literacy.	Clearer guidance and improved readability of the PL will increase patient understanding and should contribute to patient safety, treatment compliance and overall a more rational use of medicines.
V2.5.1	Develop methodologies to investigate the benefits and risks of medicines intended to promote, or manage, the health of herds.	To facilitate the authorisation of indications that benefit the herd vs the individual animals.	Could widen potential indications for veterinary medicinal products for groups of animals.
V2.5.2	Research into methods, feasibility and reliability for using social media data for detecting adverse events including under circumstances such as potential abuse, clinical errors, multiple medications, prescribing mistakes.[1]	To explore if and how use can be made of new digital technologies and communication channels (such as social media) to provide added value for the monitoring of medicines, in particular their safety.	Relevant improvement of the monitoring of medicines, including for their safety.

Number (click to send email)	Research topic	Objectives	Expected impact
V2.5.3	What are important evidentiary standards for the use of real-word evidence (RWE) for regulatory scientific advice and decision-making on the safety and efficacy / effectiveness of medicines?[1]	Develop a set of evidentiary standards to be pre-specified and used in the analysis of RWE applied to different types of regulatory advice and decisions on the safety and efficacy/effectiveness of medicines (e.g. in complement to clinical trial data in an authorisation application, or for extension of indications, amendment to product information or regulatory actions on the marketing authorisation due to safety concerns).	Developing standards will support patient access to safe and effective medicines by facilitating consistent and valid evidence-based decisions in the absence of clinical trial data or when clinical data need to be supplemented with RWE.

V3 Addressing emerging health threats and availability/therapeutic challenges

Number (click to send email)	Research topic	Objectives	Expected impact
V3.1.1	Review alternatives to conventional veterinary antimicrobials, their potential regulatory pathways and evidence requirements, and develop tools to improve and communicate these.	Review alternatives to antimicrobials, their regulatory pathways and requirements, and develop tools to improve and communicate these. Promote authorisation of alternatives to antimicrobials to reduce the need to use antimicrobials and combat AMR. Promotion of vaccines in order to reduce antimicrobial usage may be an additional point to add. To get a better understanding of the blockers to bringing to market – map regulatory and technical bottlenecks alternatives to antimicrobials (ATAMs). To understand knowledge gaps of the regulatory process among academic developers which hinder early dialogue and collaboration with regulators.	Authorisations of alternatives to antimicrobials could reduce the need for antimicrobials which would result in improved animal and public health, and would be beneficial for the environment.

Number (click to send email)	Research topic	Objectives	Expected impact
V3.1.2	Research a regulatory approach for bactericidal compounds that are not themselves traditional veterinary antibiotics.	Work within EMA and with stakeholders to develop a regulatory pathway for bactericidal antimicrobials with limited impact on public health.	Authorisations of alternatives to antimicrobials could reduce the need for antimicrobials which would result in improved animal and public health, and would be beneficial for the environment.
V3.1.3	Generate data to support authorising existing, including off-patent veterinary antimicrobials, for example, modelling and extrapolation also using PK/PD, also with the view of dose optimization (reaffirming effective dose and/or rethinking approach to dose selection).	To generate models that allow the authorisation, or maintenance on the market of antimicrobials for which there is limited economical interest but could be of interest for public health reasons.	Improved therapeutic options in veterinary medicine would allow a reduced use of antimicrobials that are also important to human medicine.
V3.1.4	Develop point-of-care and accompanying diagnostics for veterinary antimicrobial sensitivity testing.	To increase the number of VMPs authorised that are accompanied by appropriate antimicrobial sensitivity testing methods to refine the use of antimicrobials.	Refined and reduced use of antimicrobials.
V3.1.5	Conduct research to support alternative approaches for new antibacterial drug development and innovative approaches for the prevention and treatment of infections.[1]	For such developments, to optimise evidence gathering, the use of PK/PD should be exploited. Training for the EMRN should be developed to this end. Refine endpoints for serious infections, e.g. HAP/VAP. Support the establishment of clinical trials networks for such developments Re-establish international dialogue and dialogue on alternatives to traditional antibiotics.	Rapid development of new antibacterial agents in areas of unmet need related to AMR.
V3.1.6	Improve the understanding and usefulness of regulatory support to the development and application of rapid diagnostics tools (RDTs) to avoid empirical anti-microbial treatment.[1]	Promote the use of rapid diagnostics tools (RDT) in clinical trials as companion diagnostics or even co-development as the best tool to ensure rational use and avoid over-treatment.	Considerable impact on rational and personalised use of new antibacterial agents, some of which are active on single species and require the availability of RDT.
V3.2.1	Develop and apply methodology to establish Defined Daily Dose and Defined Course Doses (DDDvet/DCDvet) for other species rather than major ones, and eventually for categories of animals.	Provide reliable information on antimicrobial use per species at EU level	Providing better measure of antimicrobial use in animals with the aim of improving responsible use.

Number (click to send email)	Research topic	Objectives	Expected impact
V3.3.1	Research the mechanisms behind antiparasitic resistance, its control/prevention and which evidence should be required for antiparasitic medicines.	1. to decrease the risk of emergence and spread of antiparasitic resistance. 2. to identify the mechanisms of resistance development and transmission. 3. to estimate as accurately as possible the level of resistance depending on parasite and antiparasitic substance class.	Identify appropriate measures of prevention and control of antiparasitic resistance.
V3.4.1	Develop criteria for epidemiological modelling to demonstrate vaccine efficacy against epizootic diseases (and enzootic diseases).	1. Explore the feasibility for the use of epidemiological modelling in the demonstration of efficacy of vaccines. Establish a regulatory framework if appropriate. 2. Develop new criteria to assess efficacy of veterinary vaccines using biomarkers as a link to protection.	Epidemiological modelling and efficacy markers may be used by industry as alternative approaches to demonstrate efficacy at a population level and, for regulators, could mitigate uncertainty on vaccine efficacy in absence of field efficacy data. This could potentially reduce the costs and risks associated with the conduct of field efficacy trials and therefore would facilitate the development and authorisation of new vaccines or the addition of new indications to those already authorised.
V3.4.2	Research how regulators can interact collaboratively with industry to focus development on areas where veterinary vaccines are most needed.	To foster the development of new and/or improved vaccines for therapeutic gaps in the markets (specific target species, limited markets, zoonotic and emerging diseases).	Increase in availability of vaccines for priority diseases, limited markets; potential reduction in need for antimicrobials if vaccination is used; positive impact in animal/public health.
V3.4.3	Research how the detection of nucleic acids can be applied for the quality control of veterinary vaccines, e.g. in the detection of extraneous agents and vaccine strain characterisation.	Facilitate the development, standardisation and regulatory acceptance of new technologies (like Next generation sequencing) for the detection of extraneous agents in biological veterinary medicinal products.	New technologies may offer an alternative to replace or complement current tests for detection of extraneous agents, offering a quicker, cheaper, possibly more sensitive, simultaneous, in vitro approach for extraneous agent (EA) testing. This will reduce risks at early stages of product development when seeds need to be proven free from EAs. It also offers opportunities for implementation of 3Rs.

V4 Enabling and leveraging research and innovation in regulatory science

Number (click to send email)	Research topic	Objectives	Expected impact
V4.4.1	Develop regulatory training modules for regulatory assessors, including describing innovation of new medicines and their progression from laboratory to patient (wherever possible in collaboration with other research topics in this list)[1]	1. Identify gaps in training for regulators (done by EU-NTC already). 2. Together with EU-IN and EU-NTC draw up a list of learning objectives, key skills & competencies, knowledge & understanding to be achieved through formal courses. 3. Identify potential academic institutions that could provide courses to fill those gaps. 4. Work with those institutions, HMA and EU-IN to develop and deliver those modules.	Improved expertise of the network to provide advice and regulate more effectively and efficiently.

Methods

The methods for compiling the initial Regulatory Science Research Needs are presented below.

Source of questions

Stakeholder interviews

In the stakeholder consultations that formed the basis of the Regulatory Science Strategy to 2025,[5] interviews were carried out with chairs of scientific committees and working parties together with external experts and key opinion leaders from the EMA's principal stakeholder groups. The interviews (n = 70) were either semi-structured (55) or open (15) and interviewees were nominated by the EMRN and drawn from the Agency's expert database. Over 600 comments were received from these interviews and many of these identified the need for regulatory science research to fill knowledge gaps.

These draft research questions were then validated and added to by subject matter experts, resulting in a listing of more than one hundred draft research questions.

Review process

The EMA's internal coordination group for collaboration with academia, the 'Academia Collaboration Matrix', was used to gather further input into the draft list of questions and prioritise amongst the research areas for those to upload first into the research needs.

This EMA prioritisation was cross validated with representatives from the Healthcare Professionals' Working Party and Patients' and Consumers' Working Party and cross-checked against the prioritisation of stakeholders in the overall RSS.[2] The Healthcare Professionals Working Party were surveyed in 2021 to identify their priority regulatory science research areas.

The draft listing of research questions and the prioritisation approaches were then used to draft the RSRN list. This was reviewed by the chairs of EMA's scientific committees before finalisation and publication.

[5] https://doi.org/10.1038/d41573-019-00071-2

Options for research funding and support

EU funding mechanisms

The primary pathway to facilitating the research is envisaged to be through public funding initiatives that consider academic researchers' proposals for funding research projects covering one or more of the listed regulatory research needs topics.

The Agency is actively engaging with European Union research funding initiatives, in particular Horizon Europe[6] with the Innovative Health Initiative (IHI).[7] This engagement is aimed at raising awareness and interest in funding research questions of common interest.

The Agency is also exploring, together with stakeholders, potential collaborations with other funding organisations, at international and national level.

EMA support for research

Conduct of research on a small portion of topics may be facilitated by the Agency. Some examples of the mechanisms are presented as follows.

Research can be conducted 'in house' at EMA, involving EMA staff and external researchers as Seconded National Experts[8] or Collaborating Experts.[9] Such research may use unpublished information available to the Agency and databases to which the Agency has access, such as the EudraVigilance or electronic health record databases covering populations from several Member States. In addition, the Agency can work with stakeholders to address research questions via consultation in writing and scientific discussions at dedicated workshops.

EMA has a procurement mechanism to directly fund research questions.[10,11] Framework contractors can be funded by the Agency through reopening of the competition to contribute to research identified by EMA and the EMRN.

The EMA will also investigate inter-institutional agreements with public research organisations to conduct research from the list of the research needs.

[6] https://ec.europa.eu/info/research-and-innovation/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe_en
[7] https://www.imi.europa.eu/about-imi/innovative-health-initiative
[8] https://careers.ema.europa.eu/content/Seconded-National-Experts/
[9] https://careers.ema.europa.eu/content/Collaborating-Expert/
[10] https://www.ema.europa.eu/en/about-us/how-we-work/big-data#research-projects-section
[11] https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/monitoring-covid-19-medicines-0#observational-research-section

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Regulatory Science - Research needs
EMA/752687/2021