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European Medicines Agency

3Rs Working Party meeting report

31 March 2026, European Medicines Agency, Amsterdam

Introduction

On 31 March 2026, as part of its fourth annual stakeholder meeting, the Joint CHMP/CVMP 3Rs Working Party (3RsWP) hosted a virtual public session that was broadcast and open to all stakeholders.

The aim of this public session was to present the ongoing work of the 3RsWP, as well as the workplan priorities for 2026-2028. In addition, stakeholders were given the opportunity to comment and provide input into the working party's activities.

This report provides a summary of the topics discussed during the public session, including the input received from stakeholders during the interactive session.

3RsWP ongoing actions and achievements

The Executive Director of the EMA, Emer Cooke, opened the session emphasising the importance of advancing the implementation of the 3Rs principles and acknowledging the significant progress already achieved. As an example, she referred to the recently published qualification opinion on virtual control groups to replace concurrent control groups (CCG) in rat non-GLP dose range finding studies. It was stressed that continued progress in this area depends on strong collaboration between regulators, industry stakeholders, researchers, and method developers, working together towards a common approach to the implementation of the 3Rs principles in medicines development. It was therefore, underlined that the ambition of this stakeholder meeting was to bring together the full range of perspectives and expertise, fostering open dialogue and alignment across all parties involved.

The chair of the 3RsWP, Sonja Beken, gave a high-level overview of ongoing actions and achievements of the working party in both the human and veterinary fields of medicinal product authorisation, as follows:

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Guidance activities

An overview of guidance development activities aimed at supporting the implementation and regulatory acceptance of 3Rs approaches in medicines development was provided. Since the last meeting, significant milestones have included publication of the draft revised reflection papers on opportunities for implementation of the 3Rs principles for human and veterinary medicinal products and the publication of the draft reflection paper on reducing non-human primate (NHP) use. These documents are intended to encourage the development, submission, and regulatory uptake of innovative 3Rs methodologies.

Also highlighted was ongoing work to establish criteria for the regulatory acceptance of new approach methodologies (NAMs), including the development of a voluntary data submission ("safe harbour") framework. Revision of the guideline on the principles of regulatory acceptance of 3Rs testing approaches is progressing as outlined in the concept paper, including updates to the guideline text, annexes and a dedicated 3Rs glossary. Work is also ongoing to address comments received during public consultations on both the revised 3Rs opportunities reflection papers and the NHP reflection paper.

Looking ahead, further guidance activities are planned or underway, including revision of the guideline on local tolerance testing for human medicinal products and updates to veterinary user safety guidelines.

Stakeholder interactions

Stakeholder feedback is important in shaping EMA's 3Rs workplan and supporting implementation of the 3Rs principles in medicines development. Examples of the impact of feedback received at previous stakeholder meetings include the establishment of the International Medicines Regulators' Working Group on 3Rs (IMRWG3Rs) and the prioritisation of work on qualification and terminology. Reference was also made to the word cloud exercise conducted during the previous year's meeting, which captured participants' views on key priorities for advancing 3Rs implementation.

An update was provided on the activities of the IMRWG3Rs, which continues to support international collaboration and harmonisation on topics such as acceptance criteria for NAMs, the phasing out of obsolete tests, and the development of common regulatory positions mainly in the field of human medicinal products. The group met regularly throughout 2025 and is contributing to the development of an International Coalition of Medicines Regulatory Authorities (ICMRA) statement on the 3Rs.

In addition, ongoing EMA activities supporting 3Rs implementation were highlighted, including workshops, publications, and engagement with stakeholders through responses to media and public enquiries.

Operational activities

An overview was provided of the mechanisms currently in place to support the regulatory acceptance of New Approach Methodologies (NAMs), including activities conducted through the EMA Innovation Task Force (ITF), portfolio and technology meetings (PTMs), Scientific Advice (SA), Qualification of Novel Methodologies (QoNM), and the voluntary data submission initiative. Regarding early regulatory interaction through the ITF, trends observed in 2025 indicated a lower number of NAM-related briefing

meetings compared to previous years; however, the submissions received were considered more mature, scientifically advanced, and of increasing regulatory relevance and complexity.

An update was also provided on recent progress within the QoNM framework. In particular, CHMP issued a draft qualification opinion for a novel methodology in non-clinical research that can reduce the overall number of animals used in specific dose-range finding studies by replacing standard animal control groups with virtual control groups. Through the qualification process, evidence generated using this approach can be accepted as scientifically valid within a defined context of use in future medicines applications.

The importance of case-by-case acceptance of 3Rs approaches within regulatory procedures, including clinical trial applications (CTAs), was highlighted as a key mechanism for supporting implementation in practice. Analysis of CTAs approved between 2023 and 2025 demonstrated that NAMs are predominantly applied in primary pharmacology, particularly in situations where no relevant animal species are available. These approaches encompass a broad range of cell-based technologies and advanced models, including organoids, microfluidic systems, and other innovative platforms.

Finally, the Voluntary Data Submission (VDS) pilot was presented. The pilot represents a revision of the existing "safe harbour" procedure outlined in the Guideline on the principles of regulatory acceptance of 3Rstesting approaches, which was introduced to address the limited number of submissions received under the original framework. The revised approach provides greater flexibility by decoupling voluntary data submissions from product authorisation procedures, thereby enabling stakeholders to submit relevant data independently of regulatory applications.

The 3RsWP, through its Batch Release Testing Operational Expert Group (BRT-OEG), continued the review of in vivo quality control and batch release testing requirements for centrally authorised human and veterinary medicinal products to identify opportunities for replacement, reduction, and refinement of animal testing. The review of veterinary medicinal products has been completed, and CVMP recommendation letters have been issued to marketing authorisation holders, encouraging the use and development of validated alternative methods and other 3Rs approaches. The review of human medicinal products has also been finalised, with recommendation letters currently in preparation.

Training

The 3Rs working party provides training through various routes. These include the non-clinical and NAM European specialised expert community (ESEC), a group of experts from the European regulatory network and academia which was created to provide a platform for knowledge-sharing between experts in the field. It also serves as a pool of expertise which can contribute, if necessary, to the drafting of guidance documents on 3Rs-related topics. The ESEC hosts topic-based webinars on various 3Rs-related topics, including NHP use in safety testing of human medicinal products, read-across in non-clinical assessment, and skin sensitisation testing using 3Rs methodologies. These have been uploaded to the EU Network Training Centre (EU NTC), a learning and development platform serving the EU regulatory network. In this setting, the target audience for the trainings is assessors of human and veterinary medicinal products in national competent authorities (NCAs).

The working party is also exploring the development of a dedicated 3Rs curriculum, to be made available on the EU NTC to further educate assessors on the implementation of the 3Rs.

Non-clinical domain workplan and priorities

The 3RsWP workplan is incorporated into the EMA consolidated 3-year rolling plan for the Non-clinical domain; the latest version covering 2026-2028 was published in November 2025. This was developed taking into consideration the comments from a targeted stakeholder consultation on the draft. This consultation is an important part of the working party's continued engagement with stakeholders. Of note, stakeholder consultation feedback indicated that artificial intelligence (AI) could play an important role in the analysis and integration of NAM data, thereby supporting the implementation of the 3Rs. In response to this feedback, an AI-focused goal was added to the workplan.

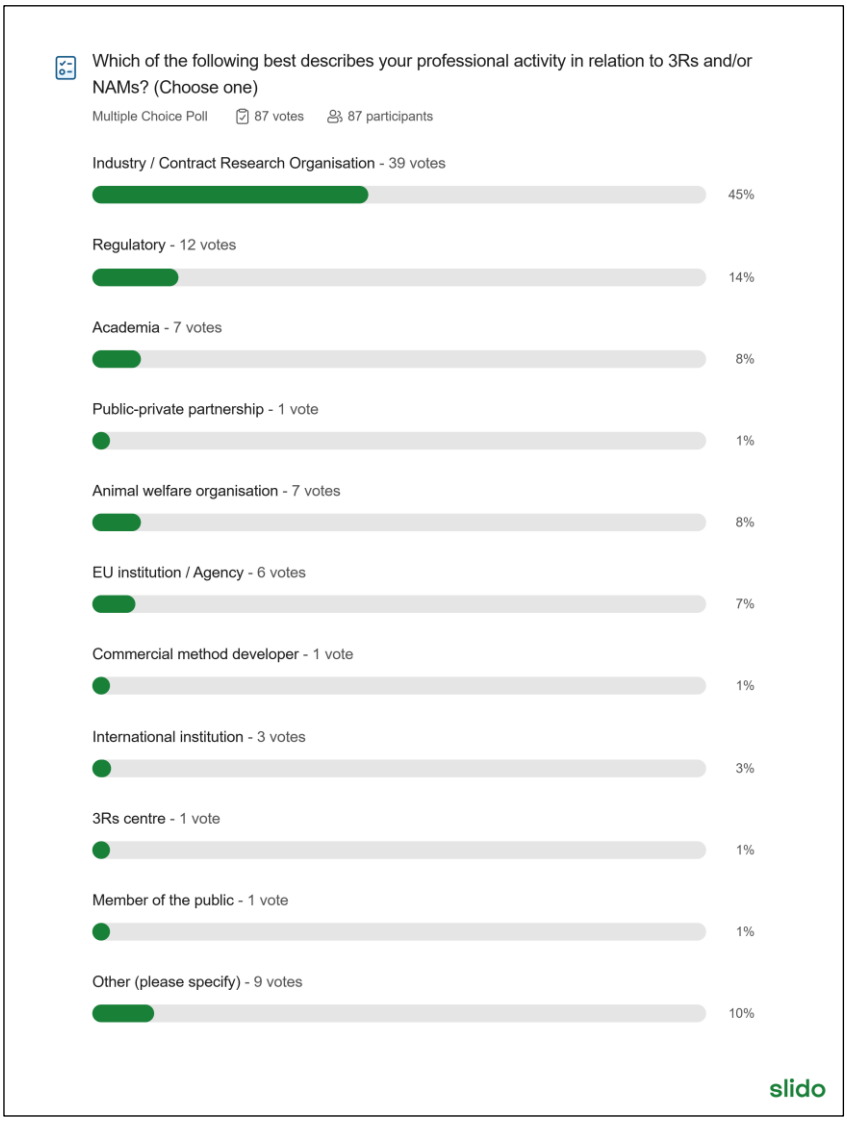
The highlights of this 3-year rolling workplan were presented, with reference to strategic and tactical goals, some of which are joint goals with the non-clinical working party (NcWP). Some activities were presented in more detail, as outlined above.

Input from stakeholders - Outcome of the interactive session

During the session, 147 participants used the interactive poll (Slido). Of those, 87 participants actively engaged with the polls and 80 responses were received for the word cloud.

Participants

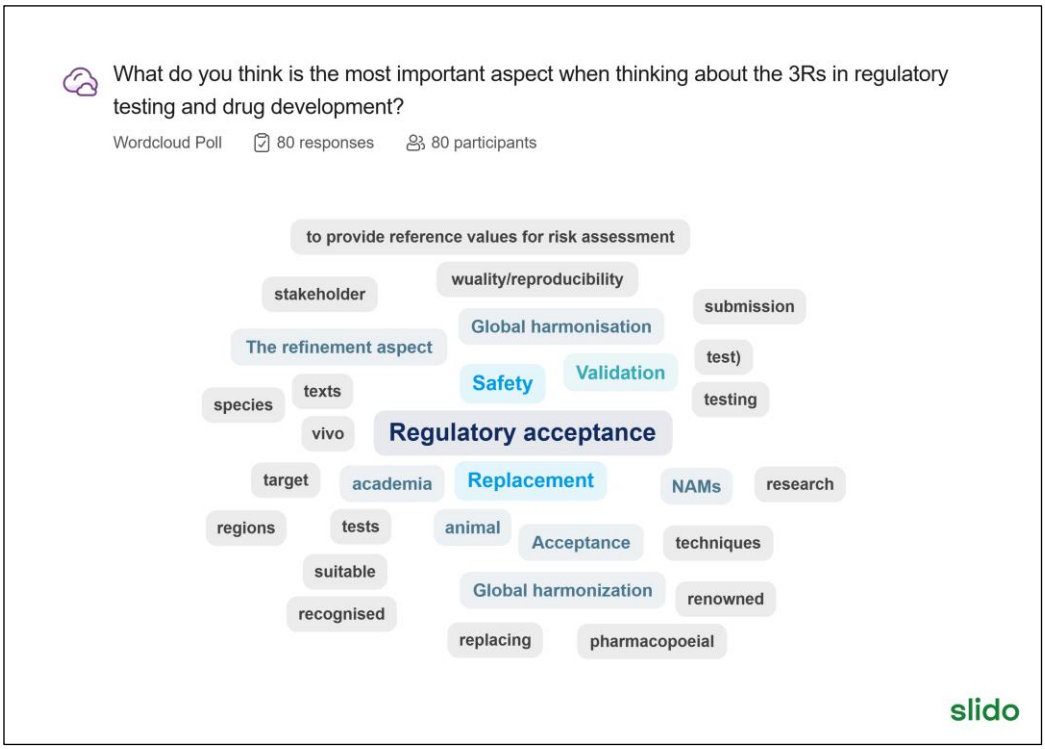
The first question aimed to understand the composition of the audience, and the results are shown below. The largest groups of participants were from the industry/contract research sector, followed by the regulatory sector. Academia, EU agencies, European commission representatives, animal welfare organisations, method developers, international institutions, and 3Rs centres were also represented. In addition, members of public-private partnerships and the general public were also represented. The 'other' category included consultants and representatives of research institutions.



3Rs aspects in regulatory testing and drug development

Participants were then asked for their opinion on the most important aspect when thinking about the 3Rs in regulatory testing and drug development. To give an instant visual impression, the results were presented as a word cloud; the larger and bolder the term, the more frequently it was mentioned by participants in their responses. Thematically, regulatory acceptance was seen as the most important aspect, which is in line with the results of the 2025 and 2024 public sessions. "Safety" and "replacement" were the second most frequently mentioned terms. The prominence of "safety" may reflect stakeholders' interest in expanding the use of NAMs in pivotal toxicology and safety pharmacology studies, where regulatory requirements remain particularly important, as well as the need for their responsible integration to ensure that patient, user and consumer safety is maintained. The strong emphasis on "replacement" underscores the continued ambition to move away from animal use where scientifically justified, while recognising that NAMs can also contribute to reduction and refinement. In addition, "global harmonisation" remained a prominent theme, reflecting the ongoing need for international

alignment of regulatory expectations and approaches to facilitate broader acceptance and implementation of NAMs, including through weight of evidence approaches.



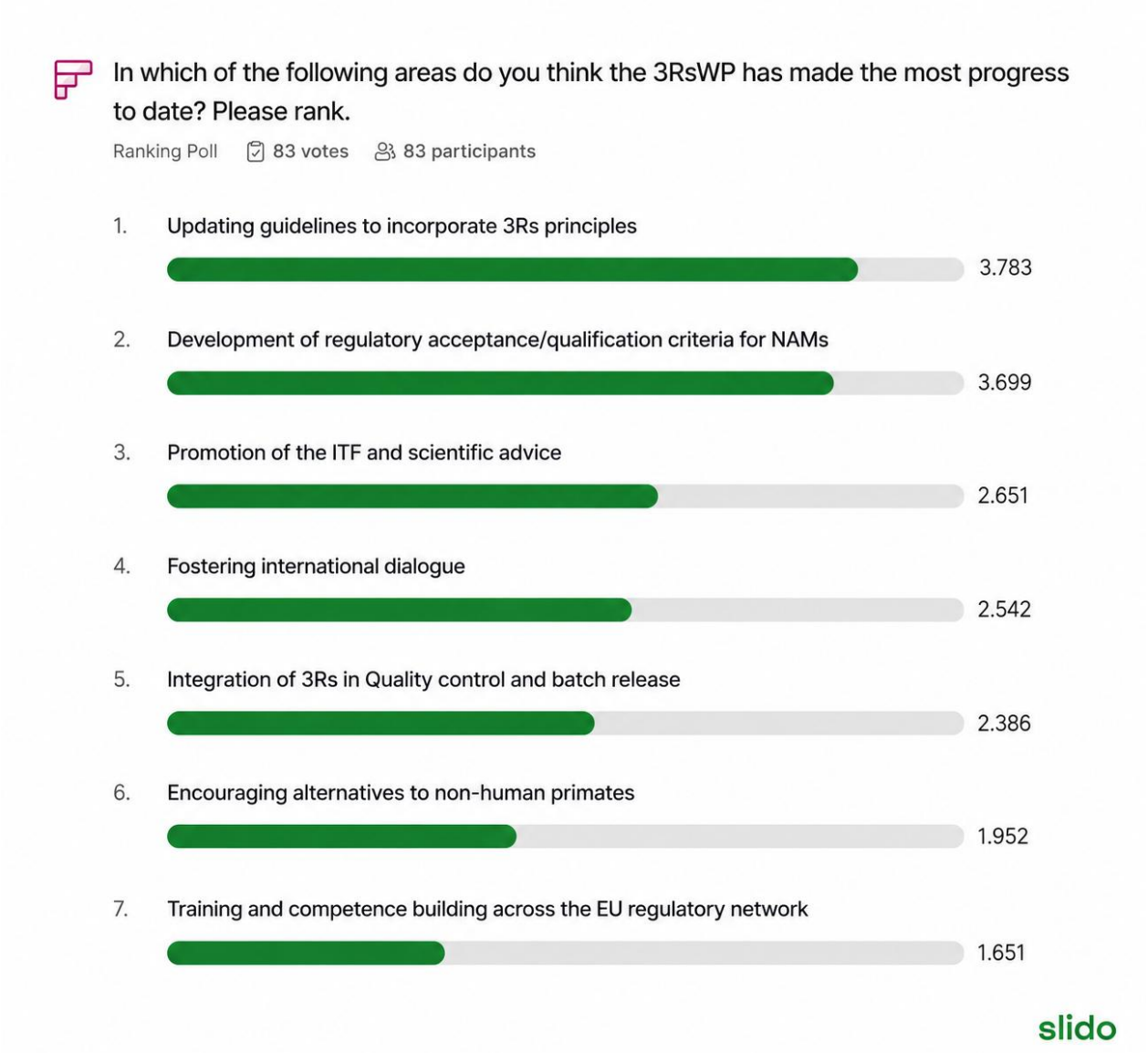
3RsWP goals

Participants were then presented with some goals of the 3RsWP highlighted as priorities for 2026 in the consolidated 3-year rolling work plan for the Non-clinical domain and asked in which areas they felt the working party had made significant progress to date. Included with each option was an example of an activity which is directly related to that goal. The results of the ranking poll showed that the most highly ranked goal related to the update of guidelines and guidance documents incorporating 3Rs principles (e.g. revised 3Rs opportunities reflection papers). This recognises the publication of the draft revised reflection papers, as described above. This was closely followed by developing and promoting regulatory acceptance/qualification criteria for NAMs, focusing on the ongoing drafting of the revised Guideline on the principles of regulatory acceptance of 3Rs testing approaches, including annexes providing acceptance criteria for complex *in vitro* models for specific contexts of use. These results are in accordance with the outcome of the ranking for 2025.

The next ranked goals were the continued procedural support to Scientific Advice and ITF meetings, as well as fostering international dialogue. Regulatory interaction pathways, such as the ITF and scientific advice, are key enablers of NAM acceptance and have seen increasing use in recent years. Raising awareness of these opportunities among stakeholders remains a priority for the 3RsWP. To assess current levels of awareness and engagement, specific questions were included in the meeting poll (see below – Mechanisms of Regulatory Interaction). Interestingly, fostering international dialogue was considered to be another area in which the 3RsWP has made the most significant progress. The focus on international collaboration is much higher than in previous years which likely reflects the global nature

of the paradigm shift towards NAMs use, and the increased awareness of the IMRWG3Rs and its planned work.

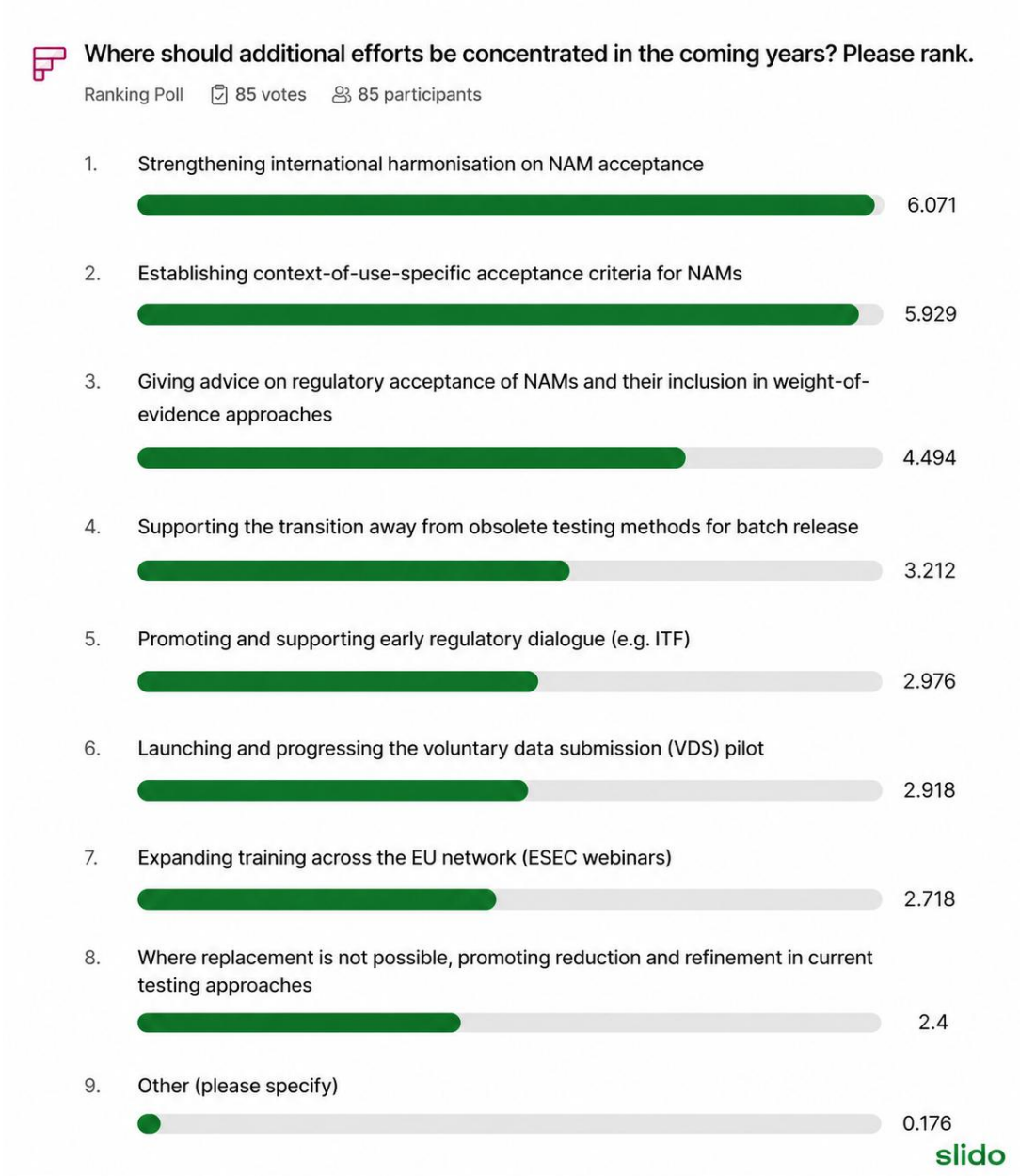
The two lowest ranked goals in terms of perceived progress were the encouragement of alternatives to the use of NHPs and the training activities on 3Rs methods across the EU regulatory network. Importantly, the draft 'Reflection paper in relation to 3Rs application in the use of NHPs', has now been published. The paper emphasises that NHP use for regulatory testing of medicines should be robustly justified and remain a last resort. It outlines opportunities for implementation of the 3Rs, with a particular emphasis on weight of evidence (WoE) approaches. It is hoped that the finalisation of this guidance document will contribute to advancing the implementation of the 3Rs in this area. Regarding the development of trainings for 3Rs methods, as mentioned previously, the 3Rs working party is engaged with the non-clinical curriculum steering group of the EU NTC and has hosted multiple NC and NAMs ESEC webinars which have been recorded and uploaded to the EU NTC as training material. As these activities are aimed at the EU regulatory network, they may be more pertinent to specific stakeholder groups.



3RsWP prioritisation areas

The next question focused on the new 2026-2028 workplan and asked stakeholders on which goals they think the working party should focus their efforts going forward (i.e. in 2027 and 2028). The top two goals were collaboration with international medicines regulators to facilitate knowledge sharing and harmonise acceptance criteria and establishing context-of-use-specific acceptance criteria for NAMs. The promotion of the acceptance of NAMs has been voted as the most important focus for the 3RsWP in all four public sessions meetings since their inception (see reports from 2023, 2024 and 2025), demonstrating the importance of this topic within the overall work of the group, and the need for ongoing activities in the area such as the 3Rs guideline revision and the continued support for NAMs-related ITF and scientific advice procedures. As mentioned above, increased focus has been attributed to international collaboration to ensure harmonisation on NAM acceptance criteria.

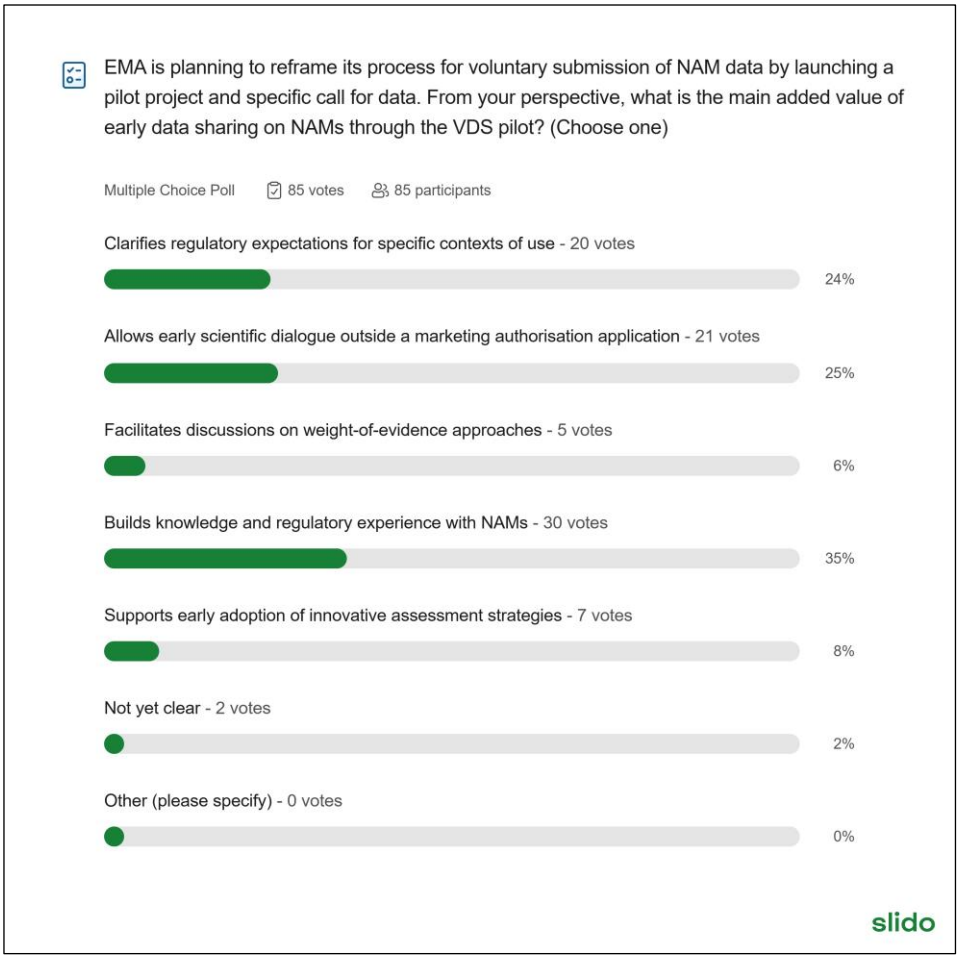
Providing advice on the regulatory acceptance of NAMs and their inclusion in WoE approaches was identified as an area requiring further development. Addressing this objective is one of the aims of the 3RsWP through the launch of the VDS pilot project, which is intended to provide participants with submission-specific, non-binding feedback on the readiness and limitations of the assessed NAMs, as well as guidance on potential next steps towards regulatory acceptance. The lowest ranked areas were training across the EU regulatory network, the promotion and support of early regulatory dialogue through ITF meetings and the promotion of reduction and refinement in cases where replacement is not possible.



Question on the objectives of the VDS pilot project

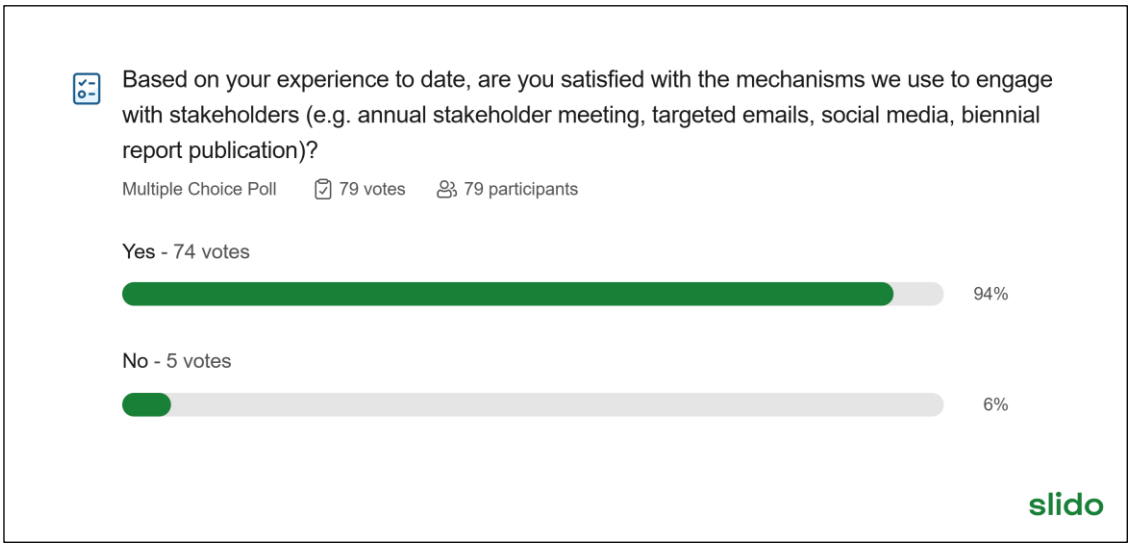
The next question focused on the objectives of the VDS pilot project. Stakeholders were asked to identify the main added value of early data sharing on NAMs through the pilot. The most frequently selected response was the building of regulatory knowledge and experience with NAMs, which aligns closely with one of the pilot's primary objectives: enabling regulators to gain greater insight into the methodologies and models being developed and how these are applied by stakeholders. The second most frequently selected response was the clarification of regulatory expectations for specific contexts of use (CoUs),

reflecting the pilot's additional aim of refining and better defining the CoUs for which submitted NAMs are being developed and assessed.



Experience with stakeholder engagement

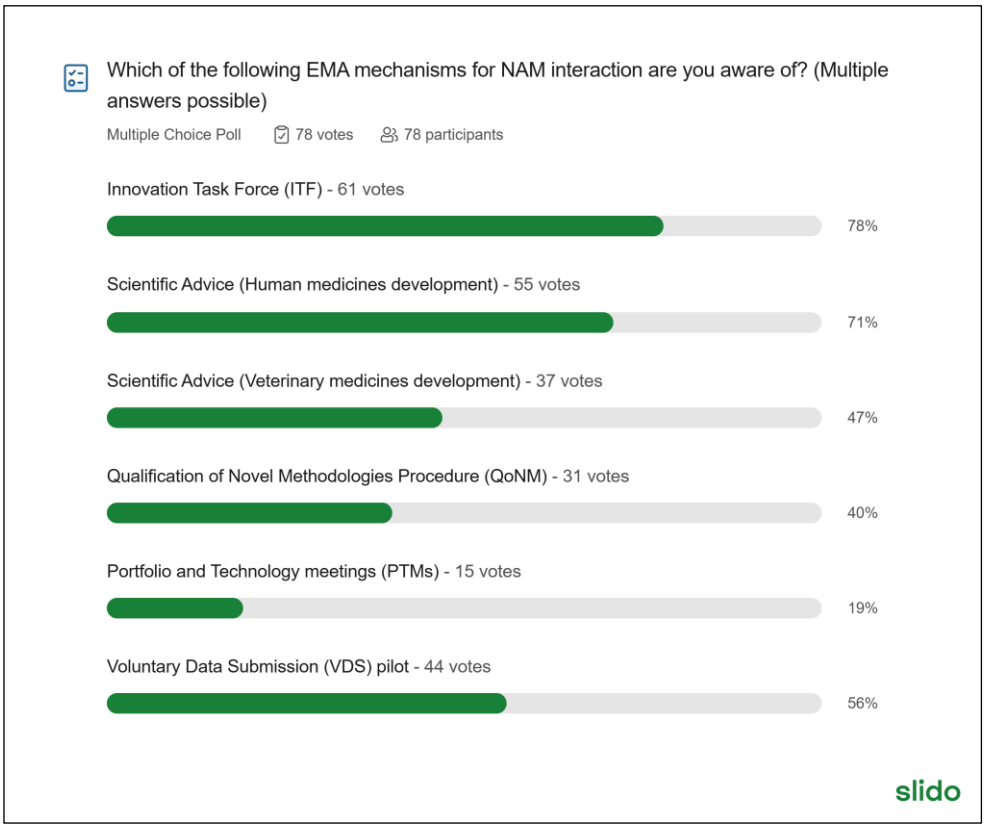
The first open question of the interactive poll explored stakeholders' satisfaction with the current engagement mechanisms used by the 3RsWP and EMA, including the annual stakeholder meeting, targeted email communications, social media activities, and publication of the biennial report. The vast majority of respondents expressed a positive experience with the existing engagement approaches. Nevertheless, approximately 6% of stakeholders indicated that they were not fully satisfied with the current strategy and provided several suggestions for improvement. Key themes emerging from the feedback included the need for increased availability for direct interaction and dialogue, earlier and clearer regulatory advice on individual strategies to replace or avoid animal testing, more timely publication of biennial reports and updates on work plan activities, greater transparency and openness of materials and meetings to the wider public, more frequent communication, and enhanced international alignment.



Mechanisms of Regulatory Interaction

Stakeholders were asked about their awareness of the different EMA mechanisms available for interaction on NAMs. The results showed that the ITF was the best-known mechanism, recognised by 78% of respondents, followed closely by Scientific Advice procedures for human medicines development (71%), while awareness of the veterinary Scientific Advice procedure was lower (47%). Awareness of the VDS pilot was relatively high, with 56% of participants indicating familiarity with the initiative. The QoNM procedure was recognised by 40% of respondents. PTMs were the least well-known mechanism, with awareness reported by only 19% of participants. However, these are specifically targeted at large pharmaceutical companies with extensive portfolios, so it is perhaps reasonable to expect that only a subset of respondents would be familiar with these. Overall, the results suggest that stakeholders are generally familiar with the more established EMA interaction pathways, while newer or more specialised mechanisms may require additional visibility and communication activities.

As a follow-up question, stakeholders were invited to share comments regarding their experience with these procedures. Most respondents indicated that, although they were aware of the available mechanisms, they had not yet made use of them.



Topics that are currently not addressed or need more focus

Stakeholders identified several areas that could be further addressed within the 3RsWP workplan. A recurring theme was the need for stronger international harmonisation and broader global collaboration to avoid duplication of animal testing requirements across jurisdictions and to facilitate worldwide acceptance of NAMs. This consideration also applies to veterinary medicinal products (VMPs), where industry stakeholders pointed to the risk that differing regional requirements for in vivo and in vitro testing could necessitate conducting both types of studies to achieve market authorisation in multiple jurisdictions, thereby increasing costs, delaying development, and limiting the potential reductions in animal use offered by NAMs. Respondents also highlighted the importance of increased training and capacity-building activities, including more visible training opportunities for regulatory affairs professionals, academia, students, CRO staff, and members of animal use review bodies. Several comments called for greater focus on specific product areas and scientific fields, including, excipients, medical devices, early drug development and efficacy testing, Phase I studies, and new modalities. It should be noted that certain topics, including alternative methods for the testing of medical devices, fall outside the scope of EMA or the 3RsWP. Additional suggestions included further work on the definition and application of WoE approaches, the role of systematic reviews and evidence synthesis, data quality requirements for regulatorily acceptable NAMs, the use of AI for NAM data integration and interpretation, and the expansion of virtual control group approaches to broader contexts of use. Stakeholders also encouraged continued efforts towards replacement of NHP use and severe animal testing, replacement of Limulus amebocyte lysate (LAL) endotoxin testing with recombinant alternatives, revision of specific guidelines, and stronger collaboration with biomedical research infrastructures and public-private

partnerships to accelerate the development and uptake of NAMs. In general, many of the suggestions are encompassed by high-level actions already described in the workplan, but the feedback was provided in more granular detail.

Concluding remarks

This was the fourth consecutive year of the 3RsWP stakeholder survey, enabling the identification of areas within the 3RsWP workplan which have consistently remained priorities for stakeholders. The importance of regulatory acceptance of 3Rs methodologies, particularly the need for clear guidance on the acceptance criteria for NAMs, has consistently been emphasised through the responses received. The feedback also indicates that stakeholders recognise the significant progress made by the working party across its broad range of activities. While there may be areas where outreach and communication could be improved, this shows that the 3RsWP workplan actions are timely and appear to address stakeholder needs. The feedback gathered through these stakeholder meetings is crucial to ensuring the continued relevance of the 3RsWP activities in supporting the further replacement, reduction, and refinement of animal use in human and veterinary medicines testing in Europe.