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Human Medicines Division
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Consolidated 3-year rolling work plan for the Non-clinical domain

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Work plan period: January 2026 – December 2028 (with a first review point after one year)

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1. Strategic goals

1.1. Short-term strategic goals

Joint NcWP-3RsWP

- Streamline non-clinical development plans for severely debilitating and life-threatening diseases beyond cancer, without compromising human safety and in accordance with the 3Rs.
- Ensure the identification and follow-up of actions related to alternatives to the use of non-human primates in line with the 3Rs and the identified shortage of non-human primates.
- Knowledge sharing and cooperation with international regulators on non-clinical and 3Rs-related aspects of assessment, and collaboration with EC and EU agencies in the food and chemical sectors to achieve harmonized approaches for hazard/risk assessment, where appropriate.
- Support and promote the sharing of non-clinical data with EMA from New Approach Methodologies (NAMs), including weight of evidence approaches, and foster their integration into the regulatory framework.
- Ensure preparedness for the implementation of the revised human pharmaceutical legislation, with a focus on environmental risk assessment (ERA), 3Rs and paediatric medicines.

NcWP

- Continue the development of approaches for assessment of nitrosamine impurities.
- Develop/implement IT tools and data infrastructure to exploit the added value of raw non-clinical data in SEND format for the re-analysis of non-clinical studies to support clinical trials, marketing authorisation and improved evidence generation.

3RsWP

- Promote and support the qualification of non-animal methods by e.g. establishing acceptance criteria for specific contexts of use and active participation in qualification procedures through SAWP.
- Encourage communication between the regulators for human and veterinary medicinal products concerning possibilities for the implementation of novel 3Rs testing approaches.

1.2. Long-term strategic goals

Joint NcWP-3RsWP

- Ensure that the breadth and depth of expertise of working party members is future-proof in relation to new emerging safety issues and therapeutic modalities, as well as emerging technologies with regards to 3Rs.
- Development of guidance addressing new demands in non-clinical assessment and 3Rs, as well as revision of existing documents.
- Identify new preclinical ICH/VICH topics in line with regulatory needs and taking into account scientific and technological progress and the 3Rs.

- Ensure the application of consistent (preferably harmonised) regulatory science on non-clinical assessment and 3Rs across different modalities by providing training within the network (EU-NTC).
- Support the integration of *in silico* methods.
- Actively track developments and use of available data in artificial intelligence (AI) related to non-clinical assessment and 3Rs, and support the integration of such methods in guidance and in practice when appropriate.

NcWP

- Assess data arising from current test strategies leading to new aspects and questions in the non-clinical domain and ensure consistency with evolving science-based non-clinical safety standards established for existing or new modalities (e.g. RNA- and DNA-based therapies, cell-based therapies, antibody-drug conjugates, synthetic peptides).
- Maintain high-quality engagement and continue building expertise to support safe and effective (paediatric) medicines development of innovative medicinal products.
- Contribute to the development, understanding of, and regulatory response to, nanotechnology and new materials in pharmaceuticals.
- Continue strengthening the interaction between non-clinical assessors and GLP inspectors to harmonise European regulatory views on GLP related challenges.

3RsWP

- Further develop the strategic role of the 3RsWP in the field of the 3Rs and strengthen cooperation between European stakeholders and international partners in the field.
- Promote regulatory integration of 3Rs-compliant methods.
- Ensure the follow-up of the application of the 3Rs in quality control and batch release testing of human vaccines, biotechnology derived pharmaceuticals, veterinary vaccines and biological medicinal products.
- Ensure compliance with Directive 2010/63/EU on the protection of animals used for scientific purposes (in the context of the relevant pharmaceutical legislation) and follow up on related plans and actions.
- Implement best practice regarding 3Rs through the review and update of EMA guidances and impact monitoring of implemented changes (including identification of new actions).

2. Tactical goals

2.1. Guidance activities

(A) Activities ongoing/to be finalised in 2026

Joint NcWP-3RsWP

- Finalisation of 'Reflection paper on the alternatives to the use of non-human primates (NHPs)'.

- Revision of the 'Guideline on non-clinical local tolerance testing of medicinal products' EMA/CHMP/SWP/2145/2000.
- Contribution to PRAC/CHMP guideline on risk assessment of medicinal products on human reproduction and lactation: from data to labelling.

NCWP

- Annex to guideline on 'Excipients in the labelling and package leaflet of medicines for human use': Finalisation of the draft information documents for the package leaflet on lactose (EMA/CHMP/186428/2016) (public consultations ended on 31 May 2019) and new revision of benzyl alcohol.
- Finalisation of 'Guideline on the non-clinical requirements for radiopharmaceuticals' EMA/CHMP/SWP/686140/2018 (public consultation ended on 30 June 2019).
- Finalisation of 'Reflection paper on the qualification of non-mutagenic impurities' EMA/CHMP/543397/2024 (public consultation ended on 30 April 2025).
- Finalisation of 'Reflection paper on lessons learnt from Covid19 about preclinical data for product development'.
- Drafting of concept paper on non-clinical requirements for severely debilitating or life-threatening diseases.
- Drafting of concept paper on the assessment of mechanism of action driven paediatric investigation plans (PIPs) in oncology.
- Drafting of concept paper on microbiome-based medicinal products to evaluate the need for harmonised non-clinical testing strategies of these products.

3RsWP

- Finalisation of the revision of 'Reflection paper providing an overview of the current regulatory testing requirements for medicinal products for human use and opportunities for implementation of the 3Rs' EMA/CHMP/CVMP/3Rs/742466/2015.
- Finalisation of the revision of 'Reflection paper providing an overview of the current regulatory testing requirements for veterinary medicinal products and opportunities for implementation of the 3Rs' EMA/CHMP/CVMP/3Rs/164002/2016.
- First revision of the 'Guideline on the principles of regulatory acceptance of 3Rs testing approaches' EMA/CHMP/CVMP/JEG-3Rs/450091/2012.
- Contribution to the revision of the 'Guideline on user safety for pharmaceutical veterinary medicinal products' EMA/CVMP/543/03-Rev.1 (to be finalised in 2026).
- Contribution to the revision of the 'Guideline on user safety of topically administered veterinary medicinal products' EMA/CVMP/SWP/721059/2014 (to be finalised in 2026).

(B) Activities to be started in 2026

Joint NcWP-3RsWP

- Collection of data to evaluate the potential need for a revision of ICH S7A.
- Collection of data on the challenges to implement revised testing strategies for biologicals in accordance with ICH S6(R1).

NCWP

- Collect data related to the challenges for the safety assessment of synthetic peptides.
- Draft revision of the ERA guideline in view of the requirements from the new pharmaceutical legislation.

3RsWP

- Second revision of the 'Guideline on the principles of regulatory acceptance of 3Rs testing approaches' EMA/CHMP/CVMP/JEG-3Rs/450091/2012.

(C) Activities to be started in 2027-2028

3RsWP

- Drafting of guidance on best practices for selecting models used for the demonstration of primary pharmacology (including 3Rs principles).
- Second revision of the 'Reflection paper providing an overview of the current regulatory testing requirements for medicinal products for human use and opportunities for implementation of the 3Rs' EMA/CHMP/CVMP/3Rs/742466/2015.
- Second revision of the 'Reflection paper providing an overview of the current regulatory testing requirements for veterinary medicinal products and opportunities for implementation of the 3Rs' EMA/CHMP/CVMP/3Rs/164002/2016.

(D) Ongoing NC domain support to (V)ICH guidelines (New/Revision/Training materials/Implementation>

- Support to ICH Q3E 'Guideline for extractables and leachables (E&L)' and related training activities for the network.
- Support to ICH S13 guideline on "Non-clinical safety evaluation of oligonucleotide-based therapeutics".
- Support to ICH Q3C 'Guideline on impurities: guideline for residual solvents' related activities.
- Support to ICH M7(R3) 'Guideline on assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk' related activities including ICH subgroup on nitrosamines.
- Support to ICH S1B 'Guideline on testing for carcinogenicity of pharmaceuticals' implementation working group.

- Develop network training activities for implementation of the addendum to the ICH S1B 'Guideline on testing for carcinogenicity of pharmaceuticals'.
- Support to ICH E14/S7B 'Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential - questions and answers' related activities including trainings to the network.
- Support to VICH activities where applicable.

2.2. Training and workshop activities

Joint NcWP-3RsWP

Develop, update and maintain the non-clinical training curriculum to ensure that availability of training courses is prioritised according to need and the appropriate level of expertise.

NcWP

- Contribute to trainings delivered during pre-clinical assessors' meetings (2026-2028).
- Develop training for non-clinical assessment of Advanced Therapy Medicinal Products (ATMPs).
- Workshop to prepare drafting of the reflection paper on the mechanism of action-driven oncology PIPs.
- Workshop to prepare drafting of the reflection paper on non-clinical requirements for severely debilitating or life-threatening diseases

3RsWP

- Develop training activities on 3Rs methods/best practices and their application and facilitate information exchange through the ESEC.
- Establish dedicated 3Rs curriculum on EU-NTC to make relevant resources available to assessors across the EU network, ensuring the 3Rs are adequately considered in regulatory procedures.

2.3. Communication and Stakeholder activities

2.3.1. European level

Joint NcWP-3RsWP

- Support the organisation of pre-clinical assessors' meetings.
- Organise annual stakeholder meetings.
- Interact with EC and IHI in the formulation of funding calls to ensure regulatory relevance of project outcomes and support their integration.
- Cooperate with the EU institutions and agencies on non-clinical safety issues and 3Rs approaches.

- Cooperate with industry and CRO trade associations for the creation and initiation of a pilot project focused on the voluntary data submission of NAMs.

NcWP

- Organise ad hoc meetings with interested parties on nitrosamines.

3RsWP

- Organise a 3RsWP-led conference to showcase achievements in the 3Rs field and identify future workstreams.
- Identify and ensure accessibility for all stakeholders to a database(s) of qualified/validated new approach methodologies (NAMs).
- Publish biennial report(s) on the application of the 3Rs in regulatory testing of medicinal products.

2.3.2. International level

Joint NcWP-3RsWP

- Collaborate with relevant stakeholders on opportunities for use of a single species in regulatory safety studies.

NcWP

- Co-chair the EMA-FDA non-clinical oncology cluster meetings.
- Support on an ad hoc basis the EMA-FDA paediatric medicines cluster for non-clinical safety issues.
- Cooperate with international regulators on nitrosamines, including contribution to ICH discussions on potential harmonisation activities.
- Strengthen the global approach to paediatric non-clinical requirements through FDA and Swissmedic participation in NcWP meetings and sharing outcomes of PIP/paediatric SA assessments.
- Cooperate with international regulators on non-clinical requirements in paediatric oncology products development.

3RsWP

- Participate in The International Medicines Regulators' Working Group on 3Rs, which aims to harmonise views regarding regulatory acceptance of 3Rs testing approaches between the EU and global regulators (https://www.ema.europa.eu/en/documents/other/terms-reference-tor-international-medicines-regulators-working-group-3rs_en.pdf).

- Cooperate with European agencies and international stakeholders involved in fostering 3Rs testing approaches.
- Maintain/update the mapping of current and future co-operations with European and international stakeholders promoting 3Rs testing approaches.
- Organise multistakeholder workshops to aid the development of regulatory acceptance criteria for NAMs within specific contexts of use, e.g. heart-on-chip for cardiovascular safety pharmacology (with reference to ICH E14/S7B Q&A) and liver-on-chip for drug induced liver injury (DILI).
- Collaborate with relevant international stakeholders to investigate the application of 3Rs in quality control testing (e.g. batch release requirements for human and veterinary vaccines).

2.4. Multidisciplinary collaboration

Joint NcWP-3RsWP

- Collaborate with CTCG regarding harmonisation of non-clinical, 3Rs and GLP related recommendations.
- Collaborate with the GLP IWG on compliance-related issues within clinical trials and marketing authorisation applications.
- Collaboration with the methodology domain to support the regulatory integration of AI and new approach methodologies (e.g. read-across).

NcWP

- Collaborate with the veterinary ERA WP, in particular with regard to interactions with the EC where EMA/network input is required, e.g. PIE strategic approach, 1S1A, review of watchlists under water framework directive etc.
- Collaborate with the Quality domain for activities (including input to QWP guidelines) related to the safety evaluation of excipients, impurities, extractables, leachables and nanomaterials.
- Foster collaboration on non-clinical issues with the Committee for Advanced Therapies (CAT).
- Collaborate with MWP and Network Data Steering Group (NDSG) on AI and PoC study to evaluate SEND implementation.

3RsWP

- Through the Batch Release Testing OEG, collaborate with the EMA Quality Domain to continue the review of product quality control and batch release testing requirements with regards to the application of the 3Rs.
- Horizon scanning to identify emerging 3Rs methods, and prioritisation of methods that are most promising and/or have the potential to have high impact in reducing, refining and replacing animals in drug development.

- Foster collaboration with the EMA Methodology Domain to support the regulatory integration of NAMs with complex data components (e.g. modelling and simulation, AI and ML, in silico and computational methods).
- Collaborate with the relevant working parties of the EMA Veterinary Domain on topics pertinent to 3Rs.
- Contribute to a working group to examine practical implications of the application of Section I.1.7 of Annex II to Regulation (EU) 2019/6 (on veterinary medicinal products) in collaboration with CVMP and CMDv.

3. Operational goals

3.1. Pre-submission activities

3.1.1. Support to SAWP

- Support to Scientific Advice and Protocol Assistance procedures on paediatric, regular non-clinical issues and 3Rs related matters.
- Support to the qualification advice/opinion for new methodologies procedures.

3.1.2. Support to PDCO

- Support the PDCO in the assessment of PIPs, with a focus on non-clinical data requirements.

3.1.3. Other

- Support to Innovation Task Force (ITF) for non-clinical aspects and regulatory acceptance of 3Rs testing approaches.

3.2. Evaluation and supervision activities

3.2.1. Support to CHMP and CVMP

- Address requests from CHMP and CVMP for input on evaluation activities.
- Contribute to product-related assessment post-authorisation following specific CHMP requests.

3.2.2. Support to other committees (CAT, PRAC, HMPC and CMDh, CMDv) and WPs

- Address requests on product-related issues, including the evaluation of safety levels of impurities.

3.2.3. Support to expert groups

NcWP

- Oversee and maintain the Nitrosamines Operational Expert Group (NS OEG).
- Oversee and maintain the temporary ICH S1B Operational Expert Group (ICH S1B OEG).
- Contribution to the Environmental Risk Assessment European Specialised Expert Community (ERA ESEC).

3RsWP

- Oversee and maintain the Non-clinical and New Approach Methodologies European Specialised Expert Community (NC NAMs ESEC).
- Oversee and maintain the Batch Release Testing Operational Expert Group (BRT OEG).

4. List of Abbreviations

Abbreviation	Definition
1S1A	One Substance One Assessment
3Rs	Replacement, Reduction and Refinement
3RsWP	Replacement, Reduction and Refinement Working Party
AI	Artificial Intelligence
ATMPS	Advanced Therapy Medicinal Product
BRT OEG	Batch Release Testing Operational Expert Group
CAT	Committee for Advanced Therapies
CHMP	Committee for Medicinal Products for Human Use
CMDh	Coordination group for mutual recognition and decentralised procedures for human medicinal products
CMDv	Coordination group for mutual recognition and decentralised procedures for veterinary medicinal products
CPCA	Carcinogenicity Potency Categorization Approach
CRO	Contract Research Organisation
CTCG	Clinical Trials Coordination Group
CVMP	Committee for Veterinary Medicinal Products
DILI	Drug Induced Liver Injury
EAT	Enhanced Ames Test
EC	European Commission
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
EU	European Union
EU-NTC	EU Network Training Centre
FDA	Food and Drug Administration
FIH studies	First in Human studies
GLP	Good Laboratory Practice
GLP IWG	GLP Inspectors' Working Group
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICH E14	Guideline on the clinical evaluation of QT/QTc interval prolongation and proarrhythmic potential for non-antiarrhythmic drugs
ICH M7(R3)	Guideline on the Assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk
ICH Q3C	Guideline for residual solvents
ICH S1B (R1)	Guideline on the testing for carcinogenicity of pharmaceuticals
ICH S5[R3]	Guideline on detection of reproductive and developmental toxicity for human pharmaceuticals
ICH S7B	Guideline for the non-clinical evaluation of the potential for delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals
ICH S13	Guideline Non-clinical Safety Evaluation of Oligonucleotide-based Therapeutics
IHI	Innovative Health Initiative
ITF	Innovation Task Force
ML	Machine learning
MP	Medicinal Product
MWP	Methodology Working Party
NAMs	New Approach Methodologies
NC	Non-Clinical
NC NAMs ESEC	Non-Clinical and New Approach Methodologies European Specialised Expert Community
NcWP	Non-Clinical Working Party
NHPs	Non-Human Primates
NS-OEG	Nitrosamines Operational Expert Group
OEG	Operational Expert Group
PRAC	Pharmacovigilance Risk Assessment Committee

PDCO	Paediatric Committee
PoC	Proof of Concept
PIE	EU Strategic Approach to Pharmaceuticals In the Environment
PIP	Paediatric Investigation Plan
Q&A	Questions & Answers
QWP	Quality Working Party
SA	Scientific Advice
SAWP	Scientific Advice Working Party
SEND	Standard for the Exchange of Non-clinical Data
VICH	International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products
WoE	Weight of Evidence