Deliverable reports

Deliverable 11. Report on omics and validation technologies. M24 (WG1-WG4).

(Action Deliverables are distinct, expected, and tangible outputs of an Action which are meaningful in terms of the Action's overall Objectives, such as reports, documents, technical diagrams, software, etc.)

Challenge/s of reference:

Challenge 2. The impact of pharmaceutics and their R&D process on the environment is high and it is responsible of huge loss due to contaminated water that affects human and animal health, generate drug resistance problems. *Integrated multidisciplinary efforts (design, synthesis/extraction, in vitro and in vivo biological/animal studies, delivery) should be developed to reduce the drugs impact on the environment at every step of the drug research and development process. This requires the coordinated action of researchers and stakeholders (governmental bodies, patients' organizations, industries and SME*.
Challenge 3. Not enough control and informed procedures are available to link the environmental impact to drug production and use. Specific guidelines do not exist to address the problem during the whole process from conception to manufacturing and use. *Concepts and strategic support in a guideline/white paper format should be given to the stakeholder in the field for a standard approach to develop safer drugs for humans and animals*.

Objective of reference (Research Coordination Objective)

Objective 3. **Coordination of the translation from *in vitro*-to-*in vivo* activities to obtain high quality leads and candidates**.

Actions: Introduction of omics technologies (genomic, proteomics and transcriptomics) and imaging for a limited number of validated leads. Drug delivery of biodegradable nanotechnology and drug targeting tools applications for both H&A R&D, pharmacology (pharmacokinetics and pharmacodynamics) on animal models by changing drug regimen and study of the effects of the different drug bioavailability tools. This can be acquired through European RTD organization and allow the achievement of high-quality leads with associated biological properties tailored for the H&A VB parasitic infections drug research program.

Working group of reference:

WG3. Coordination of *in vitro*-to-*in vivo* translation *of One Health* leads and candidates. (Challenge 3**) Objectives.** Promoting and strengthening of innovative technologies required in the translation of leads and candidates from animal to humans and vice versa to ensure the progression of qualified leads and candidates to the end of the pre-clinical phase and de-risk studies in clinical phase 1. This is restricted to advanced leads and candidate.

T3.3 *Coordination and integration of omics studies (PROTEOMICS, Genomics, TRANSCRITTOMICS) and validation technologies*, to better qualify the mechanism of action and drug resistance. All data will be deposited in the FARIDOM database. Protein targets and biological pathways from the omics studies will be validated through the evaluation of differential expression of proteins and their functional studies in cells models. (D3.3)

And

WG4. Integration of R&D process-environmental studies for the translation in informed white paper. (Challenge 4) **Objectives**: Coordination of the R&D programs innovative strategies and compliance with the overall environmental impact to provide a sharable guideline-like document. This may inform the compounds probability of exposure, an information derived from a more detailed understanding on the substances environmental fate. The validation against the ecological interpretation of selected indicators (see below) is important to properly inform drug designer and managers of environmental risks compared to societal benefits. **T4.4** *Strengthening of omics technologies as impressive possibility to identify potential molecular initiating events in organisms central to ecosystems* and their functioning. Selection of test species for these ecotoxicology experiments (D4.4). The achievements from the above studies are important for the development, validation and use of adverse outcome pathways at early stages of the design of antiparasitic drugs. The validation against the ecological interpretation of such indicators is important to properly inform drug designer and risk managers which balance amongst those environmental risks with societal benefits.

Deliverable description

Omics and validation technologies

Description of what we have done the meetings, training schools, STSM workshop performed, the *reports, documents, technical diagrams, software etc. with reference – link to the website or other external document of interest.*

In the development of new active substances, consideration of possible effects on non-target organisms is becoming increasingly important. Assessment of environmental effects is still in its infancy in drug development. Here, the One Health approach often still falls short, as environmental health is an integral part of this concept, in addition to animal and human health. Efficient, innovative but also standardizable test methods and assays are needed to assess the behavior and effects of active ingredients released into the natural environment. The application of the “omics” approach in ecotoxicological testing is at its frontier and requires careful consideration regarding the context in which the samples are collected and about standardization related to procedures adopted, including software. Data analysis is important because also at that level many software are available. Additional we include the concept of Adverse Outcome Pathway.

Meetings (information in the webpage below reported)

1. Omics technologies as a new tool in ecotoxicology. Workshop 26/03/2024 online. https://www.onehealthdrugs.com/events/scientific-meeting/omics-technologies-as-a-new-tool-in-ecotoxicology/
2. Adverse outcome pathways at early stages of the design of antiparasitic drugs 17th October 2024 - 9:00 am – 4:30 pm CET (VIRTUAL). https://www.onehealthdrugs.com/events/scientific-meeting/adverse-outcome-pathways-at-early-stages-of-the-design-of-antiparasitic-drugs-17th-october-2024-9-00-am-4-30-pm-cet-virtual/

Scientific impact (from the MoU)

- a shared experience for researchers, industry stakeholders and national/international organizations opening the way to novel fruitful collaborations for transfer of knowledge/ new knowledge creation about targets, drug research strategies, hits and leads elaboration, assays for HTS approaches, nanotechnology for drug delivery and animal studies; ecotoxicology and environmental tools applied to the research process.
- improvement of procedures and use of reagents within the green chemistry field to reduce the environmental impact;
- omics and imaging studies, with synthetic conjugation technologies and structural biology in combination with advanced molecular biology for the mechanism of action studies, new targets identification.

The long-term benefits (from the MoU

- substantial improvements of the biological profile in treating parasitic diseases caused by VB parasitic diseases affecting H&A;
- engagement of RTD platforms active in the field;
- a permanent on-line network of stakeholders in antiparasitic drug discovery and development to maintain a transfer of knowledge, new One Health knowledge creation and strengthen collaboration.

Innovation

Cross-sectorial and interdisciplinary networking approach to advance the drug discovery and development field in VB parasitic diseases in H&A (because an effective cure of the human infections can be achieved if animals' infections are cured or eliminated). Integration of the innovative approaches with the environmental impact concepts, will involve also pharmaceuticals manufacturing and use.

The Action will facilitate such innovation through active promotion of the database (IP regulated) and search for collaborators in academia and industry. IP on new advanced candidates with promising or relevant pharmacological activity will be promoted.