1. Summary for publication: 2nd project period (1.1.2019 – 31.12.2019)

1.1 Summary of the context and overall objectives

The pharmaceutical industry in particular, as well as the advance of biomedical science in general, depend on robust data and scientific rigor as essential for efficient decision making, patent strength and reducing time-to-market/deployment, which in turn determines knowledge gain and availability of new treatments to patients. Recent publications report challenges with the robustness, rigor, and validity of research data, which may misinform decisions about whether to proceed to further preclinical or clinical testing as well as questioning the predictability of preclinical models.

We will propose simple, sustainable solutions to facilitate data quality without impacting innovation and freedom of research. Our consortium is pooling resources from academia and industry to pilot this action in Neuroscience and Safety, but with applicability beyond these R&D areas.

The European Quality In Preclinical Data (EQIPD) consortium is

(i) defining those variables in study design and data analysis that influence outcome in pre-clinical neuroscience (focus on Alzheimer's disease and psychosis) and (neuro-)safety studies conducted in industry; and establish whether these are the same variables which influence outcome in academia;

(ii) defining the components of the EQIPD quality management system;

(iii) defining consensus quality management recommendations for non-regulated R&D;

(iv) validating the feasibility of the quality management system in prospective studies;

(v) delivering an online educational platform providing certified education and training in the principles and application of quality and rigour.

We are conducting systematic reviews and meta-analysis of historical data sets from industry and academia to identify features of study design which influence outcome in preclinical studies. We have used a Delphi approach to reach consensus around core principles for preclinical robustness, and will validate these approaches in cross site experiments and establish ring testing experiments in non-regulated research. We are developing a quality system framework to allow researchers to demonstrate best practice and a governance system to ensure sustainability and relevance.

We are also developing an educational platform to ensure research community-wide expansion of knowledge on criteria and principles necessary to address robustness and quality.

Junior researchers are involved in many of the tasks and are enrolled in an academia/industry joint exchange scheme.

1.2 Work performed from the beginning of the action to the end of the period covered by the report and main results achieved so far

We continue to make good progress across Workpackages: WP1 functions as an effective project management structure and oversees implementation, communication and dissemination. WP2 has made very good progress in converting identified datasets for analysis, now almost complete. Systematic reviews of published data in AD are progressing, with 230,000 identified citations, good performance of the machine learning algorithm, and data extraction in meta-analysis ongoing. WP3 has completed the review of existing recommendations and identified the key principles of preclinical research quality; the draft framework is now with other WPs for testing. Their systematic review has been accepted for publication in an open access journal. In WP4, localisation and harmonisation stages are complete, and planning of the final ring testing stage is underway. WP5 has defined the scope of the new quality system, and the development of that system is almost complete: beta-testing of the tools and mechanisms to support the implementation and performance monitoring of the new quality system with key external stakeholders is underway. WP6 have developed a monitoring and assessment system for the new quality system, as well as developing a prototype governance system. This work is informing active discussions about the status of the EQIPD QS after the IMI funded period. WP7 has hosted summer schools for young researchers, made good progress in establishing the exposure section of the learning environment and some progress in establishing the education

section of the learning environment. Again, sustainability of training provision beyond the funded period is a focus of current discussion. WP8 have formulated a transparent protocol for unbiased inclusion of experimental paradigms and datasets, developed the EQIPD Data Warehouse, making good progress in implementing a reproducible data pre-processing process, identified the characteristics for a persisting data sharing platform, and is engaging with FAIR-plus to support appropriate data availability. WP9 has extended its scope and has created an animal care and use questionnaire that has been completed by most consortium partners. Responses are analysed and communicated to the other WPs.

1.3 Progress beyond the state of the art and expected potential impact (including the socio-economic impact and the wider societal implications of the action so far)

The systematic review and meta-analysis of a large volume of historical industry data is unprecedented, and will allow us to establish whether the problems with rigour identified in the published literature also apply to industry data. Preclinical safety data (with focus on Irwin test) are rarely published so the systematic review and meta-analysis of historical industry safety data will again be unprecedented. Our results will inform the extent to which strategies to improve rigour should be targeted to areas of specific weakness or should be generalised.

The development of tools to improve research rigour will allow involvement of research providers at different stages of improvement. Researchers will be able to shape their improvement strategy in the light of their current performance. Involvement of key external stakeholders will facilitate dissemination and implementation. Finally, the development of standard approaches to ring testing and the demonstration of the feasibility of a strategic and organised approach to multicentre efficacy studies represents a major advance.

EQIPD will have expected impacts on (1) improved European citizens' health and well-being, (2) improved data quality of pre-clinical studies, (3) contribution to animal welfare: 3Rs + robustness, (4) enhanced intellectual property protection and regulatory success, (5) a cultural change in the implementation of quality principles in preclinical science, (6) building confidence between research partners, and (7) facilitation of collaborations through common quality standards.

In particular, we have increased the potential impact on animal welfare and the 3Rs by establishing an additional working group specifically charged with exploiting opportunities to enhance the ethical position of animal research. While the systematic review of guidelines was not targeted at guidelines relating to animal welfare, the search terms used allow re-use for this purpose, and this is something we hope to return to in later stages of the project.

The systematic review of guidelines for research conduct has already had unforeseen beneficial impacts; we have shared these with the US NIH and with a group established by the Australian NHMRC. Both agencies are considering training requirements for in vivo researchers and considered our review to provide a basis in evidence for the choice of components of a core curriculum. We are hopeful that they and others may endorse our guidelines, so that there is a globally agreed core curriculum. This would allow training providers (including SMEs) to develop materials secure in the knowledge that there would be substantial demand for their product.

1.4 Address (URL) of the action's public website

www.eqipd.org