Autumn
2021

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Tackling the replication crisis: European science leads the way

The Enhancing Quality in Preclinical Data (EQIPD) project is a €9-million IMI (Innovative Medicines Initiative) project to bring more rigour and reproducibility to preclinical research. The project kicked off in 2017, and the formal part is now coming to a close. Here Project Leader Dr Thomas Steckler (Janssen Pharmaceutica NV), is interviewed about the EQIPD project's achievements, by ECNP Press Officer Tom Parkhill.

Tom Parkhill: Dr Steckler, EQIPD has now run for four years, and the formal part of the project is coming to an end. How will you follow up the project?
Thomas Steckler: We have spent a lot of time to ensure that what we have developed is sustainable, and we are in the process of setting up a society. It's currently at the German Tax Office – which is interesting! They required a physical, inaugural meeting, so we recently had a small formal meeting in Heidelberg, and now we are just about up and running. It will be a new society, based in Heidelberg (at least from a tax perspective). We'll start the society with a core group from the EQIPD consortium, to get it going and to develop a society strategy. We'll also have an operational arm outside the society, which will do the assessments and acceptance of sites.

Let's go back to the beginning. What was the need?
People had begun to realise that we faced an inherent difficulty in non-clinical research. There was a problem with low reproducibility in the published literature. There was also a problem in traceability, being fully transparent, having good documentation, and so on. Based on that, we realised that we needed to take some action. We couldn't really rely on data which was not robust, and you can't build hypothesis and develop your own research programmes, if you can't follow up the work, the publications. One of the key issues that we (and others) did identify was that the quality of many pre-clinical datasets was relatively low. Either because the data generated had relatively low rigour – perhaps no blinding or randomisation, perhaps not all data was shown, perhaps it was difficult to compare published data to raw data – and so we thought we would need to develop this quality system, which is now the cornerstone of our output from the EQIPD project.

What are the most common mistakes people make which result in poor quality data?
It's difficult to put a finger on it, because if people don't report something, you don't know *why* they have not done so. Hasn't it been done, or have they just neglected to report it? One common mistake is that people run an experiment in a particular way because they have always done the experiment like that. For example, with sample size calculations people may say "we've always used 10 samples, so we'll use a sample size of 10 again", and they never reconsider whether n=10 is sufficient. And so you have studies which are not really robust enough to be reproducible. The philosophy we have in EQIPD is that you should run highly rigorous studies, for example including randomisation. But there might be reasons why that is not feasible. That's OK, but if you haven't done it, then report that you haven't done it, say why you haven't done it. A second aspect is under-reporting. People read something and try to reproduce it but fail, because the recipe is incomplete. These are critical aspects.

Who has supported the EQIPD project?
We initiated the consortium in October 2017. We now have 10 academic partners and 12 EFPIA (European Federation of Pharmaceutical Industries and Associations) partners, and we have eight small-medium sized entities, which also includes ECNP as a learned society. We now have around 100 stakeholders in total. This includes interested individuals, but also research groups or institutions which followed what we are doing, and in return gave us feedback on whether we were on the right track. So we have an interested community. We also have some associated collaborators, groups which were interested and which wanted to contribute on a voluntary basis, even after the consortium was put in place; this meant that they didn't receive any direct benefit from IMI (Innovative Medicines Initiative), but were able to contribute.

And what has EQIPD developed?
We have developed a quality system which is lean and flexible. It can be set up over time. We have some basic requirements, but the rest of the system is set up in such a way that people can take what they need in their special situation. Some research units may want to implement everything, others may only need specific aspects, so they won't spend more time than is needed on the quality system. We have a full infrastructure, and everything that we have developed will be freely available. The quality system is published, and we have some online tools, which help with the setup of the systems and provide some additional information. People can to a large extent proceed at their own pace. They can have a self-assessment (we have developed a questionnaire), so they don't need to share the assessment with anybody. But of course they *can* share it, they can also ask advice from the operational arm of EQIPD. The final level would be a formal assessment, which is a more in-depth evaluation by the operational arm. This could take the form of a remote assessment, but it could also include an onsite assessment. We can't visit every lab, but we'll pick random labs, and they will get a visit. In that way we hope that people will stick to the principles of the quality system.

At the end, there is a certification process – if you

have been assessed and accredited you will get a certificate. We envisage that this will be valid for a three-year cycle. This will cost of course, but we're not looking to make money, it's to cover the running costs – travel, hotel, etc.

Can this accreditation be used, for example, on publications?
Yes, we are looking into different options. We have received interest from some of the big science R&D service providers, companies like Scientists.com and Science Exchange. These companies have links to a huge number of research groups. They have their own quality assessments already implemented to ensure people work according to certain standards if they say so. Now they are looking to implement the EQIPD processes and encourage partners to at least do the self-assessment, and possibly to go for the accreditation. And these organisations, if they pass the assessment, can use the EQIPD logo. We think this will make these companies more attractive partners, to pharma companies for example. We are also talking to some funders about whether they would be interested in applying the system: it may be an added benefit when you apply for funding if you can say "Look, we are EQIPD-accredited", it shows the funder that there is a certain rigour in your processes.

So it's like CE mark. Of course you come from a background in neuroscience, but the systems seem more generally applicable.
That's right, like a CE mark. But it's not limited to neuroscience; we just started there because we had to start somewhere. It wasn't that neuroscience had any greater need than other fields, it was just that many of the people who joined forces to propose EQIPD had a neuroscience background, and we could tap into that infrastructure. But the output from EQIPD is more generally applicable. We'd like to view this as a quality mark, maybe somewhat comparable to AAALAC accreditation for animal care and use programs, but in the non-regulated non-clinical space.

Your output at the moment is the online work platform…
We have different outputs. We have the online training platform, which is conceptually finalised (there have been Covid-related delays). It will be made publicly accessible, probably in the next couple of weeks. Then we have the training activities, which have been relatively successful. We started with the summer school. We joined forces with the workshops arranged by the ECNP's preclinical data network. Earlier this year we had a virtual workshop with close to a hundred participants from all over the world – it was really nice. We've also had interest from other groups. We ran a session for the Finnish neuroscience community, and at the moment we're pulling together a training session for some scientists in Brazil (this is one of the good things about virtual activities – location doesn't matter). Finland is building its own reproducibility network at the moment, and they reached out to us.

In 2020 we also published a handbook on *Good Research Practice in Non-Clinical Pharmacology and Biomedicine*, with many contributions from EQIPD. This book can be downloaded for free here.

Now I guess you need to get more buy-in, especially internationally.
EQIPD started as a European project, but we have interest from the US and EQIPD members in the US. And of course, the big R&D research companies are globally active. We've made a good start!

For more information on EQIPD, see https://quality-preclinical-data.eu, http://www.eqipd.online or https://eqipd-toolbox.paasp.net/wiki/EQIPD_Quality_System.

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This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777364. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.
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