

Developing Exploratory Programmers Based in India

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ABSTRACT

Interest in cost reduction motivates pharmaceutical companies to collaborate with programmers located in emerging countries like India. However, cultural differences and differences in work habits have to be bridged in order to successfully team up with such countries. Additionally, effective exploratory and post study analyses impose special requirements on statistical programmers. The process of exploratory work at UCB for one of its products is briefly outlined, and a training concept is introduced that has successfully been applied at UCB, to integrate programmers from Accenture, based in Mumbai, India, into an exploratory statistical programming team. Finally, a train the trainer approach is presented, which in the future will be used to develop programmers for exploratory work on site at Accenture.

INTRODUCTION

About five years ago Statistical Programming at UCB decided to collaborate with functional service providers for statistical programming support on new and existing clinical studies with UCB remaining in full control of the process. This included the application of UCB SOPs and the use of UCB standards on UCB servers. Therefore most studies were led by an internal statistical programmer from UCB who would oversee a team of external programmers. These programmers consisted of either expert contractors from western countries or contractors from vendors having a presence in emerging countries (e.g., Accenture India) that could provide a more cost efficient model. UCB subsequently implemented a new strategy for the conduct of studies with strategic partners which included all statistical programming activities for those studies. With the implementation of the Strategic Partner model for clinical studies, UCB is better suited to focus its statistical programming on key competencies such as submission activities, post-hoc exploratory analyses and other post study activities (e.g., publication and payer support). Such exploratory analyses in particular can be quite different from standard study-related statistical programming and requires a special skill set. This paper describes UCB's approach to develop statistical programmers in Mumbai, as part of our partnership with Accenture, to acquire the needed skills to successfully implement exploratory analyses and how the entire training concept has developed thus far.

BACKGROUND OF EXPLORATORY PROGRAMMING AT UCB

UCB recognizes that innovative and creative aspects for progress of knowledge and value of its drugs often stems through the need for specific analyses of databases whether internal or external. It is also recognized that a sound rationale for such analyses may be originated by various professionals within the company or from external interests (e.g., Key Opinion Leaders, Advisory Boards, or Payers).

Thus, there is a need for data generation activities, to deliver scientific knowledge that is:

- of high scientific quality and integrity
- within the overall project strategy
- planned and resourced for timely delivery
- published as relevant according to Global Publication Practices

I will refer to these activities as exploratory analyses or Data Generation Team (DGT) requests afterwards. At UCB DGTs have been assembled for established brands to cover these needs. They work on requests if no special team exist, as for example it is the case for submissions, safety signal detection, market research, or epidemiological analyses. Typically DGTs are supporting congress contributions, scientific manuscripts, advisory boards, data mining initiatives, validation of new methods of measurement such as questionnaires, support for health economic analyses, support for value dossiers, support for health technology assessment projects, support for study planning, and more. At UCB DGT teams consist of a chair and core members, among them a lead biostatistician, a statistical programming lead, a publication manager, and medical representatives. For specific requests, adhoc members can be added as needed. Accenture statistical programmers were integrated into a DGT programming team of in total 18 full time equivalents. This programming group has an overall lead and five sub-leads for different "missions". In this context, missions can be thought of to be roughly equivalent to different indications. For mainly historical reasons, the DGT workflow is slightly different for each mission. Programmers occasionally have to switch between the sub-teams and consequently be prepared for each workflow. In 2013, this DGT provided approximately 4,200 outputs for which approximately 350 analysis datasets had been created because clinical study report

analysis datasets alone were not sufficient. to fulfil the requests required for the missions. This is clearly a large volume of activities that surpasses the activities of any one clinical study.

PLANNING THE TRAININGS

When planning to develop programmers from Accenture into DGT programmers, the first step was to describe the typical kind of requests/activities that are performed in DGTs at UCB. Since almost all programmers from Accenture at UCB had been assigned to clinical study work before, in doing this it was deemed helpful to contrast DGT work with the study work. The next step was to identify the special skills that are needed by programmers to successfully and efficiently manage these tasks. By comparing these skills with the skill set of the programmers from Accenture, a training plan was derived.

EXPLORATORY STATISTICAL PROGRAMMING AT UCB

The most striking difference between exploratory and clinical study work is related to the quality of evidence that is gained. In study work, results for primary (and often secondary) endpoints are controlled with respect to statistical error probabilities whereas exploratory analyses are not testing any hypotheses in a strict sense but should rather be considered as hypothesis generating at most. This is of relevance for a programmer, for example, when it comes to judge strange results that simply might be due to a very small number of subjects contributing to an analysis. Another big difference refers to the workload. DGT work is not as constant as study work is. When study work starts, a programmer pretty much knows what he or she will be doing three weeks later. However, the course of work in DGT programming has its peaks and troughs, culminating before congress submission deadlines and calming down in between. In addition priorities can always be rearranged and work can be interrupted by urgent high priority tasks such as responding to health authority questions. Study work and DGT work also differ with respect to the work flow. When programming starts for a clinical study, the protocol and the Statistical Analysis Plan (SAP) are in place and rarely will change during the course of programming activities. Timelines are fixed, as well. However, a DGT request might not be completely specified in the beginning but rather be the starting point of a development process. Depending on first results, the research question could be refined during several review cycles so that in total working could last for over one year with several breaks in between. Another important difference between study work and DGT work is versatility with respect to many aspects. DGT programming teams can work on several requests in parallel stemming from different indications of the same compound. Not just one study could be involved but many and sometimes even all studies of a compound (e.g., cross-indication safety analyses). This requires being familiar with the protocols of each study and not with only one. Working with data from different studies also means that different programming environments can be involved (e.g., for legacy studies). Therefore DGT programmers have to be familiar with several workflows. In addition, DGT programmers usually collaborate not with just one study biostatistician but with several biostatisticians. Content wise, DGT requests cover a much broader range of tasks than study work. This corresponds to a very broad range of statistical methods. Depending on a research question, programming specifications of a DGT request can vary drastically. For large requests, specifications can be similar to study SAPs but may also consist of just one sentence for small tasks. Contrary to study work, where usually only the lead programmer is in contact with the study team, in big DGTs, programmers must be prepared to collaborate with other DGT team members

SKILL SET OF EXPLORATORY PROGRAMMERS

The key skills that every DGT programmer should have, in addition to skills required for study work, can be defined (please see first column of Table 1. Certainly, many of these skills must be qualified to be ambitious. It is clear that some skills can hardly, if at all, be developed by training alone even if it lasts several weeks. This is hands-on experience someone gathers, especially when working for several years on the same compound. UCB does have programmers for whom this is true. Nevertheless, knowledge transfer is possible to a certain extent and this was done as part of the training.

TRAINING CONCEPT

When starting to think about the training concept, it soon became clear that simply setting up a syllabus would not be enough. Some more general aspects of the training needed to be considered, as well. One very important part of the training concept was its long-term perspective. Statistical Programming at UCB wanted to start the training project by developing a group of programmers to the extent that they could act as trainers of their Mumbai based colleagues later on. In order for the training to be beneficial and gain the on-the-job experience, it was determined a stay of several weeks onsite at UCB (in Germany) was necessary. It was UCB's hope that a long stay abroad would also allow working on possible issues related to cultural differences (ICUNet.AG 2014). All programmers from Accenture had already worked together with lead programmers from Germany or the USA and therefore were already accustomed to work in a global team. However, it was our understanding that collaborating with contract programmers from Europe in a twin role for either development or validation of TFLs likely would need further development. The same was true for contributions in meetings. Finally, UCB was well aware that being away from families, friends, and colleagues for a long time could become an issue and therefore planned for every endeavour to organise the day to day life of the Monheim visitors to be as comfortable as possible.

TRAINING PLAN

Accenture managers agreed to look for candidates for the training who should have the potential to develop the skill set described. They should speak English fluently and should have gathered solid hands-on experience in clinical study work at

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UCB before. After internal discussions within UCB it was decided to apply the training modules displayed in the second column of Table 1. Table 1 does not present the training plan in its timely order but rather describes the modules and how they relate to the key skills needed.

Table 1 Skill set of exploratory programmers and corresponding training modules

SKILL	TRAINING MODULE
Ability to work in a global team	• Experience of collaboration and interpersonal relations among colleagues in Monheim • Attendance at DGT meetings as guests • Focussed discussion with trainer about expectations on DGT programmers where cultural differences are involved (critical thinking; speaking up; contributing to team discussions; etc.) • Using “Focussed discussions” as training method
Understanding of drug development process, scientific and experimental thinking	• Focussed discussions with trainer about basic scientific concepts (e.g. scientific terms; definition; operationalization; objectivity, reliability, validity) • Focussed discussions with trainer about the drug development process with anecdotic information • Presentations by Accenture programmers about goals, design, and results of selected studies important for DGT work with discussion • Presentations by Accenture about proposals for the design and analysis of studies they would develop with discussion
Understanding the “big picture” of the compound	• Presentations by Accenture programmers about the diseases which are treated by the compound with discussion
Knowledge about the compound and its studies	• Presentation by Accenture programmers about the compound and the indications where it is administered • Presentations by Accenture programmers about goals, design, and results of selected studies important for DGT work. Subsequent discussion with expert programmers.
Knowledge of the DGT workflow	• Presentation by trainer about DGT structure and process as well as it's environment • Discussions with UCB internal experts of the content areas DGTs cover • Passing a DGT e-learning course • Study work (SOP about scientific publishing at UCB)
Ability to quickly understand study designs	• Study work about the compound in general (Investigator Brochure, e-learning courses about the compound, etc.)
Ability to make sense of purely specified requests	• Focussed discussions with trainer with real life examples from the past
Advanced knowledge of statistical methods	• Internal training in Mumbai • Presentations by Accenture programmers about results of analyses with advanced statistical methods they had not used before (e.g. longitudinal modelling) with discussion
Ability to deal with legacy structures and content	• Presentation by trainer

IMPLEMENTATION OF THE TRAININGS

The whole project is now in its third year. Three groups from Mumbai consisting of three programmers each have been trained. Two groups have been to Monheim, the first group for three months and the second group for two months. The third group was trained in Mumbai by programmers who had been in Monheim before. All programmers met the expectations of UCB's programming group with respect to their professional background. The Monheim trainings were supervised by the DGT overall programming lead who also acted as the trainer most of the time. During these trainings three to four one and a half hour long sessions took place each week. The remaining time was used for the preparation of presentations and homework

(e.g., reading) if time allowed because the programmers had to fulfil other professional obligations in parallel to a small extent. Some of the training modules had to be conducted sequentially. Others were performed when an occasion arose. Overall, the training in Mumbai also took place over a period of two months. The statistical trainings were conducted by external vendors (SAS India). The programmers from Accenture in Monheim started with actual DGT work after about half of their stay for less complicated or urgent requests. They soon worked together with expert programmers based in Europe. As had been expected by UCB's statistical programming group, at the end of their stay they confirmed that having been able to watch their Monheim colleagues interact and work had been very informative for them. With respect to their well-being, UCB took care that they could prepare their meals at their accommodation and at work. Lucky enough, a supermarket with all Indian groceries is not too far away from Monheim. They were fully integrated in the everyday life of the department., shared office space with Monheim colleagues on their own desks, and participated in departmental activities. UCB employees living near Monheim invited them to trips to the vicinity or other extracurricular activities. They kept in close contact with their families, friends, and colleagues in Mumbai. They also took the chance to visit European metropolis like Munich or Paris. Shortly before their leave, a farewell party was organised where they were presented with a certificate about their successful training as exploratory programmers.

AFTER THE TRAININGS

After their trainings, the first two groups were on a level that could be expected from a newly hired expert contractor. After one and a half year of working in the DGT, two programmers from the first group were also able to support the involved biostatistician to write an analysis plan where only a vaguely framed research question was available in the beginning. However, as expected the trainings could not compensate hands-on experience fully. Integration of the third group who had been trained by Accenture in Mumbai was not as seamless as it had been for the first two groups. For this reason it was decided to extend the training concept by adding weekly meetings with the whole Accenture DGT team. These meetings are intended to discuss any issues that might have occurred during the week and to conduct additional training modules when appropriate. For example, in order to ensure that errors do not occur, the programmers are trained to interpret the results. Together with the DGT biostatisticians we also plan to have a monthly meeting where common statistical methods are introduced with data from studies which are currently analysed. Over time, a collection of presentations will be built up that can be used for future trainings in Mumbai. In addition, UCB plans to send a trainer to Mumbai later this year for two weeks to deepen training contents and to discuss the training procedure in Mumbai.

CHALLENGES

One of the important challenges mentioned earlier relates to the improvement of the trainings conducted by Accenture in Mumbai. Another challenge concerns turnover of staff which happens in India much more often than in Europe or the US.

CONCLUSION

To our knowledge, it has been the first time in the industry that programmers from India have been trained in Europe for several weeks to acquire the skill set that's needed to successfully work in exploratory programming. This ambitious objective was fulfilled. However, UCB-Statistical programming also aimed at the implementation of a train the trainer process. Currently this is on-going with still room for improvement. Nevertheless six of the eighteen full time equivalents currently working in one of the biggest DGTs at UCB are programmers from Accenture. This contributes to an efficient use of financial resources considerably.

REFERENCES

ICUNet.AG (2014): "Intercultural Preference Tool" [available at <http://www.icunet.ag/en/the-icu-solution/intercultural-assessment/iptr/>]

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