IMI – 7th Call 2012

Evaluation of Stage 2
March 2013

Independent Observers' Report

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Table of Contents

Abbreviations:

EFPIA - European Federation of Pharmaceutical Industries and Associations; IMI Innovative Medicines Initiative;

EoI - Expression of Interest; FPP - Full Project Proposal

1. Background

This is the report of the independent observers for Stage 2 of the 7th Call for proposals by the Innovation Medicines Initiative (IMI). The 7th Call was launched 17th July 2012 and submission of proposals in response to the 2 Themes was invited: -1st Call theme: "Developing a framework for rapid assessment of vaccination benefit/risk in Europe" and -2nd Call theme: "Incorporating real-life clinical data into drug development". The IMI website accepted Expressions of Interest (EoIs) in response to the Call up until a deadline for submission 9th October 2012.

The resulting Expressions of Interest (EoIs) submitted by applicant consortia were evaluated in November 2012, leading to the selection of one highest-ranked EoI for each topic. This marked the end of 'Stage 1' of the 7th Call. . The results of these evaluations were communicated to applicants in Dec 2012. In Stage 2, the consortium responsible for generating the highest-ranked EoI for both Call topics were then invited to join together with the matched consortium of EFPIA member companies, forming a larger project consortium which together would submit a single Full Project Proposal (FPP)- one Consortium for each of the two topics.

The two FPPs were then evaluated by independent experts, first through remote evaluation between 8th and 21st March 2013 and then in panel discussions in Brussels 25th and 26th March 2013. Discussion by the expert panel for Topic 1 took place on the 26th March and for Topic 2 on the 25th March. In parallel with these discussions, independent ethics expert reviewers held separate discussions on the two topics in adjacent rooms. Both sets of experts were supported and the meetings chaired by members of the IMI JU Secretariat. The Stage 2 evaluation process ended with the generation of consensus evaluation reports for the FPP for each consortium, which were then communicated to the applicants.

2. Overall observations

The observers found that, as with the Stage 1, the Stage 2 evaluations were conducted professionally and fairly and according to the established procedures and regulations. Both observers were struck by the dedication of all participants to ensuring an impartial and thoughtful evaluation of all EoIs. The IMI team once again performed an outstanding job in publishing and publicizing the Call, organizing the EoI submission and evaluation process, contacting highly professional and well qualified professionals and in putting together the onsite evaluation meetings. As highlighted below, further improvements in the procedures from the previous Calls were implemented. The clarity of the onsite briefings for evaluators was especially appreciated as well as the excellent organization and coordination of the process. The observers were very pleased to see that the 2 day process was set up according to the plan and the panels for the 2 topics ran smoothly according to the pre-defined agenda.

In our opinion:

- There were no violations against the rules of the published evaluation guidelines. The evaluators were of a very high quality and carried the relevant expertise for each of the topics.
- All participants approached their tasks professionally.
- The evaluation of the FPPs, and the discussions in the panels, were exhaustive, frank and fair.
- The continued use of 'Hearings' were organized in a very effective manner and appeared universally welcomed and it was efficient to assign individual questions to particular panel members to ask the consortium representatives.
- The opinions of all experts on a panel were considered (also those participating remotely through Teleconference) and discussed in equal terms while making the final decisions.
- There was good interaction between the Ethical Review panels and the Scientific/technical Review panels.

- The Consensus reports were drafted with active participation of all evaluators and reviewed collectively, under the guidance of the IMI project officers to ensure the comments and recommendations were in line with the scores.

3. Role and approach of the independent observers

3.1 Role of the independent observers

As stated in the IMI's *Rules for submission, evaluation and selection of Expressions of Interest and Full Project Proposals 3.4*, the role of the independent observers is as follows:

"The role of observers is to give independent advice to the IMI JU on the conduct and fairness of all phases of the evaluation sessions, on ways in which the experts apply the evaluation criteria, and on ways in which the procedures could be improved. As such, they shall verify that the procedures set out or referred to in these Rules are adhered to, and report their findings and recommendations to the IMI JU. They are also encouraged to enter into informal discussions with the IMI JU staff involved in the evaluation sessions and to suggest to the IMI JU any possible improvements that could be put into practice immediately. However, in the framework of their work, they should not express views on the expressions of interest and full project proposals under evaluation or the experts' opinions on the proposals."

3.2 Working method of the independent observers

In performing their task the independent observers had access to all written information supporting the Stage 2 evaluation process, and access to the SOFIA environment. They attended both days of evaluation sessions at the Crowne Plaza meeting rooms in Brussels 25-26 March 2013. While there, they attended the briefing sessions, sat in on the panel discussions- both the Ethical Review panel as well as the Scientific/technical Review panel, and spoke individually with many of the expert evaluators present. They also had ample chance to speak with IMI employees, including the Scientific Officers acting as moderators, with IMI lawyers, the IT support specialist and with Michel Goldman, the Executive Director of the IMI.

4. Observations and recommendations

In the following sections we record our observations on the Stage 2 evaluation process, we note improvements in the process compared to that for previous Calls, and give some recommendations for modifications which we feel might benefit the process for future Calls. These observations and recommendations should be read against the background of our general comments in section 2 above, where we express our overall opinion that the evaluation process has been well, carefully and fairly implemented throughout and that the overall process is of excellent quality and follow international peer review standards.

4.1 Preparation of the Full Project Proposals

The preparation of the FPPs following the choice of the top-ranked EoIs during Stage 1 evaluation is a demanding task. Within the space of around 3 months, the coordinators (in most cases coming from EFPIA member companies) are required to bring together the full consortium and then lead it to generate the FPP. The time allocated for this process is rather short, however on this occasion as previously it was generally considered to be feasible.

For one of the topics, requirements given by the expert panel at stage 1 that needed to be addressed during FPP preparation were particularly challenging, as they related to getting public health bodies involved in the project. The IMI Executive Office had acted as a neutral platform to facilitate such interactions during the FPP preparation phase, without taking part in the discussions and negotiations.

Recommendation 1:

It would be useful if the winning consortium produced a written document as an Appendix outlining their response to the reviewer's comments showing how they tried to address them if they are not covered in the FPP.

4.2 **Remote Evaluation Stage**

Following the generation of the FPPs, the expert evaluators had around 10 days in which to evaluate them remotely. This process worked very well for the scientific and ethical evaluators and was facilitated by a briefing session. All evaluators were able to provide full reports prior to the face to face meetings on the 25th and 26th of March.

As recommended in an Independent Observers Report of a previous Call, the ethical reviewers now have timely notice, a clear brief and read/write access to all of the information from Stage 1 to enable them to begin summarising comments ahead of the FPP and ahead of the Stage 2 panel meetings. They now also have a dedicated form within the SOFIA environment.

The observers were further pleased to see a comprehensive description of the role of the EFPIA participants in the Call, with the result that EoI consortia were better able to match their work plans accurately with the possible contribution of EFPIA consortium members.

Recommendation 2:

Consideration should be given to the comments of the ethics panel on the automated tool and possible solutions implemented.

- In terms of the ethics report form having only a 'Yes' or 'No' the ethics panel felt that these two categories were not enough - there needs to be the opportunity to grade the response in the same way as the expert scores are (good/fair etc) and qualify them.
- It was also mentioned by that panel that in the Stage 1 ethics review there were no subcategories which might be helpful in giving more specific feedback if issues were identified at that stage.

Recommendation 3:

Could the IMI give some consideration to having a 'pool' of reviewers which have already been briefed, ahead of time, to the IMI processes and, for groups like patient groups, some education in the nature of the scientific review process. For Topic 2, one of the panel members, who was there as a patient group representative, felt the time allowed for review was too short and much underestimated especially for people new to the process. This is especially so when projects are of a general nature and not focused on a specific therapy area.

4.3 **Expert evaluation panels**

The experts in the evaluation panels were selected and invited by the Scientific Officers as described in "Rules for submission, evaluation and selection of Expression of interest and Full Proposals, 3.2". All experts fulfilled the criteria stipulated there and the high quality of the individuals present pays tribute to the efforts of the IMI Scientific Officers in securing a good mix of people for each panel (an especially hard task given the difficulty of finding suitably-qualified expert evaluators who are not involved in any applicant consortia and were not subject to any kind of conflict of interest). The mix of the panel ensured a balance such that no one person monopolised the debate and everyone contributed to all the discussions, apart from when they had to withdraw due to stated conflicts of interest.

The composition of the panels were essentially the same as that in the Stage 1 evaluation, however due to availability and conflict of interest issues some new panel members had to be added to one of the expert panels.

Issues of potential conflict of interest were taken seriously by the IMI staff, with the entire panel and in the presence of the IMI Director, arranged time for a round with open discussion in which each evaluator of the panel was invited to declare and explain any potential conflict of interest situations and how they would be dealt with. These were reiterated by Fatiha Sadallah from the IMI on the 25th and Michel Goldman from the IMI on the 26th.

IMI director Mr Goldman and the IMI staff took sufficient time to explain the rules (eligibility, participation), evaluation process and the decision making process, including impartiality and the various types of conflict of interest for which the evaluators should be alert. Also, to avoid any interference between the two panels dealing with the 2 different topics, the evaluation panel discussions took place on two different days. This obviously contributed to consistency in the evaluation decisions and to the very constructive and open discussions in panels, as observed. Most of the evaluators were thus already familiar with the project to be evaluated, the considerations of the panel in Stage 1 and with the views and expertise of each other. Panel members were also aware of the nature and goal of the evaluation process, their responsibilities, the choices available to them and the consequences of their decisions and recommendations. Rapporteurs had been appointed for each panel for each Topic prior to the meeting which worked well.

The basic structure for the onsite panel discussions was as follows:

1) Each panel member was invited to briefly describe his/her main points of concern about the proposal and then the panel formulated a list of questions for the Hearing session with project coordinators,

2) The EFPIA and academic representatives/coordinators of the consortium received these questions shortly beforehand as they arrived in Brussels and were then invited into the room with both panels (Scientific/technical and Ethics) present to give a short presentation and to answer questions and comments posed by members of both panels, then

3) Both panels of expert evaluators worked separately on the preparation of their recommendations and the consensus evaluation report.

In all sessions, the expert reviewers brought specific knowledge, perspective and commitment to the discussions with the result that each FPP was critically examined and clear recommendations made. Considerable time was spent preparing a list of very detailed and well structured questions that were to be addressed during the hearing session. Much effort was made to improve the proposals and adjustments were suggested that would not have been possible without meeting face to face. Preparing the questions, discussing those with the applicants as well as defining adjustments and recommendations was a very beneficial result of the onsite evaluation. Since the

implementation of recommended adjustments to the FPP falls to the responsible IMI scientific officer, the active involvement of the scientific officers in the evaluation discussions is of critical importance. As noted in our report on Stage 1, we were again pleased to observe that this involvement was aided by the provision of administrative support for the scientific officers.

One evaluator participated remotely through teleconference, which generally worked fine, although a few times the connection broke. As stated above, the Ethical Review panel held their meeting in a similar manner, but in a separate room close by. This allowed the two panels to work in parallel, but have easy contact and present their questions to the other panel.

One panel member in one of the topics stated that he remained unhappy with the Stage 1 review process – his comments were investigated by the independent observers and they concluded that they were unfounded and were not supported by other panel members.

The quality of the panel rapporteurs was excellent – they were especially effective in resolving conflict where one panel member held very strong views.

Recommendation 4:

It would be desirable for the scientific experts to have site of the draft ethical review ahead of the hearing with the Consortia, especially if there are ethical issues

Recommendation 5:

The separation of the ethical and scientific review panels worked well for working up issues and the consensus document, but it would be good to have the ethics panel or at least the relevant ethics rapporteur to sit in on the discussion with the Consortia.

4.3.1 **Hearings**

The observers were pleased to note the continued use of an onsite Hearing. Questions were sent briefly before the Hearing to allow them to reflect and be prepared to some extent. The expert panel received the recommendation that the hearing questions were meant only to clarify certain key issues to help with consensus scoring and ranking, not to collect entirely new information. During the Hearing the questions were read out by each of the panel members in turn. These Hearings were extremely useful in providing the panels with a deeper understanding of the strengths and weaknesses of the proposals. We strongly recommend the continuation of this practice.

Recommendation 6

As per the independent observers report for Stage 2 of the 6th Call, it would be good to continue the practise of allowing the Consortia some early sight of the questions on the day – even for 15-30 minutes, especially where there are lot of issues. Could any major ones be flagged even earlier since the evaluator reports come in some days beforehand?

4.4 Consensus Evaluation Reports

The panel chose one chair from its members who led the development of the list of questions for the Hearing and the writing of the consensus report. During the Hearing the panel adhered to the timing set and to the scope of the questions prepared jointly. After the Hearing the expert evaluators then finalised their scores and

recommendations to form a consensus evaluation report and the ethics review panel finalised their consensus report. The panels took a considerable amount of time to work on the final recommendation and the consensus Evaluation Report. Because the reports were made jointly during the panel sessions they reflect well the view of the entire panel of evaluators and in general the panel members quickly reached agreement on the main points.

4.5 Budgeting

No serious budget issues were raised by the evaluators for Topic 2. A question on budget was raised for Topic 1 and it was made clear to the Consortia that even if the EFPIA in kind contribution would increase, the budget for the non-EFPIA members of the consortia was capped at euros 5M.

4.6 Ethical Review

As noted above, a panel of ethical experts had access to the SOFIA environment to contribute to the FPP evaluation. We appreciate that the ethical review panels were invited and fully participated in the process at Stage 2, and that the ethical reviews had the chance to interact with the other scientific/technical review panellists, as we noted that this increased their level of understanding on ethical issues and how deep the impact could be on a project. We highly recommend that this arrangement is continued.

4.7 Interim Review

As in previous calls the nature and timing of interim reviews, as well as this time the timing of an ethics audit, was requested.

The independent observers reports from Call 4 and Call 5 had made specific recommendations that, during the generation of the FPPs, the coordinators should be required to generate a series of (4-5) 'High Level' Deliverables, relating to the objectives in the Call Topic, against which project progress will be reviewed at the Interim Review level. We were pleased to see that this was implemented again in this Call 7 Stage 2 FPP and we make the on-going recommendation that this continues with future Calls. Although not possible under the current IMI regulations, one could consider coupling these deliverables with the authorization of transfer of part of the budgets based on a positive outcome of the Interim Review - depending on the recommendations of a Scientific/technical Review panel. Obviously it would be beneficial to invite experts from the Scientific/technical Review panel to assist with such an Interim Review, as they would be better placed to judge the progress from a scientific/technical perspective.

4.8 Moderation of the expert evaluation panels by IMI

As with previous Calls, the evaluation sessions were moderated by Scientific Officers from the IMI office. Once again the Scientific Officer was given considerable support by another member of the IMI office staff, with a dedicated IT officer and with two lawyers available throughout the sessions relieving them of some of the administrative burden and allowing them to concentrate more fully on their role as moderators and to answer directly any questions regarding potential conflict of interest from the evaluators. All Scientific Officers fulfilled the essential and often difficult role of moderating the evaluation panels with intelligence and fairness, and the

standard of moderation across panels was seen to be relatively homogeneous. Moderators answered evaluators questions rapidly and supplied information where needed, helping the panels to reach an impartial consensus. Signs of the effectiveness of the moderators' handling of the panels were the observations that the experts functioned as teams, working well together and that the writing of the consensus reports proceeded smoothly. Once again, the IMI Lawyers were on hand to read all consensus reports and ensure that the language used was well aligned with the scores. The observers were pleased to note that moderators encouraged the team of evaluators to explore clearly outlying scores in greater detail to make sure that a key point is not being missed, that comments made by independent evaluators who could not be physically present in the consensus discussions were taken into account as well and that the overall wording reflected the scores and ranking.

4.8.1 Remote evaluation

As noted above not all independent evaluators were able to be present at the evaluation sessions in Brussels, but their comments were readily available for everyone and the scientific officer made sure these were taken into account through the discussions. As has happened before in a previous call, the use of a camera to relay the proceedings in the room would really add to this and is certainly warranted in case there is a stable connection with sufficient bandwidth.

The online submission and evaluation system appeared to have functioned effectively without technical problems.

All independent evaluators were able to see the other evaluators' (however anonymized) scores and comments to allow better preparation for the onsite evaluation meetings.

5. Overall conclusions and comments

Both these Topics were particularly challenging in their nature and scope yet they represent the types of areas that may be explored by IMI or Horizon 2020 consortia in the future. It was gratifying that solutions to issues raised were in the main found and that both projects were recommended for progression.

The following recommendations were made:-

Recommendation 1

It would be useful if the winning consortium produced a written document as an Appendix outlining their response to the reviewer's comments showing how they tried to address them if they are not covered in the FPP.

Recommendation 2

Consideration should be given to the comments of the ethics panel on the automated tool and possible solutions implemented.

Recommendation 3

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As per the independent observers report for Stage 2 of the 6th Call, it would be good to allow the Consortia some early sight of the questions on the day – even for 15-30 minutes, especially where there are lot of issues. Could any major ones be flagged even earlier since the evaluator reports come in some days beforehand?

Other Comments

(as already recommended in the Call 7 stage 1 report): as the broader aim of IMI is to make strategic changes in the entire sector, it is clear that other stakeholders than the usual projects partners (academics, SMEs, EFPIA members) should be involved more deeply in the projects were appropriate. For example, dissemination of new methodology will not ensure adoption and implementation of those methodologies in practise. Also, they need to be recognized by the regulators as valuable and eligible in the regulatory process. Moreover, these innovations need to be to the actual benefit of the patients, HTA schemes need to recognize the added value for Healthcare Outcome and national reimbursement schemes need to be ready and willing to pay back. This goes towards recognition that Innovation is needed beyond the product or service level with clinical value, but involves also a focus on socio and economic parameters that affect uptake and market.
The 2 topics under Call 7 already move in that direction in which CROs, patient organizations, regulators (EMA, ECDC) and HTA organizations were specifically mentioned in the call text and invited to participate in the consortia. Practical problems could arise if one specific key organization (e.g. EMA) then has to be present/be invited into competing consortia in order to be eligible for receiving funding. An alternative option could be to set aside a special budget line (of a few %?) from the IMI budget, not from its overheads and separate from the call funds and at the discretion of the IMI Board, to be allocated to support the active involvement of such key stakeholders to the consortia that go through the first stage evaluation (top up their project budget). Flexibility to include non-traditional participants if required might also be necessary e.g. if diagnostics or medical devices become important for a particular proposal.

Commentary of 2 US expert reviewers, in context of comparing IMI (EU) funding with US (e.g. NIH) funding:

- positive quote: “in the US there is a much stronger tendency of “defensive writing” in anticipation of what specific reviewers are likely to say than in Europe and usually have a more linear approach, while in Europe there is a much more focus on planning what you want to do. Also here there is a stronger emphasis on achieving a high level of integration of the most relevant stakeholders into the consortia.....”

-positive: “there is here more flexibility with (management and admin) rules than in the US system .....”

6 Acknowledgements

The independent observers were helped in their task by all participants in the Stage 2 consensus meetings, and they would like to thank the independent experts for being so amenable to being 'observed', and for all the conversations that helped so greatly in the formulation of this report. In particular they would also like to thank the IMI staff for their help before, during and after our stay in Brussels for the consensus evaluation meetings.