IMPRESS: Improving exposure assessment methodologies for epidemiological studies on pesticides

1st Project Advisory Board meeting, 15th December 2017

IOM, Edinburgh, UK

Agenda

Time	Item
08.30-09.00	*Arrivals / coffee*
09.00-09.10	Tour de table
09.10-09.30	Project governance and role of Advisory Board(AdB) *(Karen)*
09.30-10.00	Overview of study aims and objectives *(Ioannis)*
10.00-10.40	WP1 progress and discussion *(Hans)*
10.40-11.00	*Coffee*
11.00-13.00	Progress and discussion on WP2 and WP3 *(Kate and Ioannis)*
13.00-13.30	*Lunch*
13.30-14.00	Continue discussions on WP3 *(Ioannis and Kate)*
14.00-14.30	Dissemination activities *(Karen)*
14.30-15.00	~~Collaboration with other researchers~~ Feedback from Advisory Board
15.00-15.30	Next steps / AOB
15.30 -	*Departure*

Documents circulated prior to meeting:

- Agenda (above – item crossed item and replaced just prior to AdB meeting)
- Description of work
- Project governance document
- WP2 protocol_version 5_2 for AdB

Powerpoint presentation used at meeting

Attendees:
Advisory Board: Aaron Blair (AB), Silvia Fustinoni (SF), Len Levy LL), Mark Montforts (MM)
Project team: Karen Galea (KG), Ioannis Basinas (IB), Martie van Tongeren (MvT), John Cherrie (JC), Andy Povey (AP), Kate Jones (KJ), Johan Ohlander (JO)
Apologises*:* Roel Vermeulen, Anne-Helen Harding
Meeting Chair: Aaron Blair
Minutes: Karen Galea

Tour de table

Qu - Are the Advisory Board (AdB) expected to produce a report following the meeting? It was agreed that the AdB would produce a short written report. Action: AdB to provide written report to accompany meeting minutes. Update following meeting and minutes being finalised: Done.

Project governance and role of Advisory Board

It was agreed that it was good that the project team had a project governance (PG) document in place and that the organisation was clear to see. There was extensive discussion concerning the contents of Appendix 1 (Advisory Board terms of reference) in the PG and several requests for amendments / clarification were made which are summarised below.

- Section A3 – It was considered that there should be explicit mention that the members of the Advisory Board should not have a conflict of interest in relation to the IMPRESS project (e.g. currently working for ECPA (European Crop Protection Agency), collaborators) and if they do, they should declare it. It was agreed that a conflict of interest form would be circulated for members of the AdB to complete ACTION: IOM to circulate a conflict of interest to AdB members for completion and include text in PG concerning this form. Update following meeting and minutes being finalised: Done.
- To ensure transparency, the PG document should also be displayed on website and this was agreed. Action; agreed updated PG document will be placed on IMPRESS project website.
- Section A5 - It was discussed that to ensure independence the AdB should decide who acts as Chair and deputy Chair, rather than the Management Committee. It was agreed that this would be changed. Action: AdB to advise the IMPRESS investigators who will act as Chair and deputy Chair. Update following meeting and minutes being finalised: Done, Aaron Blair (Chair), Mark Montfort (Deputy Chair)
- Section B4 – It was considered that there should be clarity on what information is actively being generated and made publically available. It was agreed that the AdB would not check data, but it did encourage data to become publically available. The project team advised that ECPA encourage making data publically available and that the project team intend on doing so via supplementary material with project publications. It was also highlighted that public availability of the data will be made available (with due consideration of any data protection requirements) once the project team have finished published their work resulting from the IMPRESS project. It was agreed that the following text would be added to section B4 of the PG *…."with a view to ensuring timely publically availability of relevant data".* Action: Amend PG. Update following meeting and minutes being finalised: Done, PG has been updated with an appropriate statement,
- It was agreed that while the AdB would advise on publications, their role is not to authorise or approve them. It was discussed and agreed that publications should be circulated to the AdB for final review after being commented on by ECPA.
- It was discussed that there should be noted in the PG document that AdB members are allowed to communicate to others that they are members of the AdB. The project team advised that the names of the AdB have already been communicated (e.g. through website and conference presentations) and that the AdB members can communicate this role as they see fit. Action: additional bullet point to be added to Appendix 1 of PG. Update following meeting and minutes being finalised: Done
- There was a lot of discussion concerning point D5 and particularly with respect to redaction of material from the minutes. It was considered that the sentences concerning redaction should be removed and that the minutes should be documents that can be publically shared, and as such

they would not contain any sensitive information or preliminary results. With this is the understanding by the AdB that their comments regarding the design and conduct of the project would be fully included in the minutes. Action: update PG to remove reference of redaction. Update following meeting and minutes being finalised: Done

- Appendix 2, Section B2 – changed 'agree' to 'advise' which was agreed. Action: Update PG. Update following meeting and minutes being finalised: Done.

The project team highlighted that the PG forms part of the overall contract between IOM and ECPA and so will also need to be agreed by ECPA before being finalised.

Action: Remove 'Prof' title from IMPRESS project website for Aaron Blair. His designation at NCI is "Scientist Emeritus."

Overview of study aims and objectives

Slides were viewed and there were various questions raised concerning the studies being included in the IMPRESS project (some of these points were more relevant to WP2 and WP3).

- PIPAH (Prospective Investigation of Pesticide Applicators' Health) – are they farmers? They are professional applicators (had to be trained and registered). Do they have records? Yes, but there is no central repository for applicators to place their records.
- Could agronomists help provide information? It was considered not, as doubtful they could disclose information given to farmers and it was unknown whether they would keep this historical information.
- There was some confusion concerning the PIPAH study and which participants were being considered for the various work packages. The team advised that current self-reported active sprayers from PIPAH will be recruited for WP3 (biomonitoring) and we will approach the whole population to participate in WP2 (questionnaire) i.e., (the full 5700 PIPAH participants).
- It was raised that there may be an issue with PIPAH people being continually asked to participate in a study however it was highlighted that from the IMPRESS project perspective we don't need that many.
- Electronic / paper questionnaires? For this project we will administer the questionnaires as far as possible in the same manner that they were originally administered. Exceptionally the electronic copy of the PIPAH questionnaire will not be used because its utilisation in previous survey was very poor previously. No other cohort uses an e-questionnaire.
- AdB viewed the PIPAH questionnaire and commented that it was very long and complicated.
- The Ethiopia study was discussed. This includes a large group of exposed people who are re-entry workers. Do we find that different pesticides are being used or pesticides that are being phased out? Found some being used which have already been phased out in Europe. It was raised that a big issue for WP2 is the enormous turnover of applicators and the strong possibility that we might not be able to re-interview previous participants.
- SHAW study – Conducted 234 in-person interviews 10 years ago, but due to the age of the group a significant proportion will have died.

The AdB made the general observation that we are using a lot of different pesticide exposed populations, which are all very different. Pulling them together in a coherent way will be difficult and it will be challenging to produce a guidance / general model. The project team responded that the type of exposure assessment applied in a study will depend on the study design and endpoint of interest. It was acknowledged that it will be hard to come up with generic advice, but that general information for individual studies would be given. WP4 will look at how we can improve or not, by making easy changes that result in more robust algorithms.

AdB highlighted that being able to re-interview people about exposures for the same time period and determine how consistent responses are for each study will be valuable. It should also be possible to look at this by different age groups, i.e. do young people recall better than older people?

Qu - Are we using questionnaires from other studies? No.

AdB highlighted concerns about applying results from one study to another study and doubted that this would be possible. Thus, the utility of a questionnaire to assemble information on pesticide exposure in a location different from where it was developed provides information regarding the effectiveness of that questionnaire in a new region, but it does not provide information regarding the reliability and validity of the instrument in the region for which it was developed. Response was that this is not the projects intention.

AdB thought that it made sense to establish how well exposure assessment was done in the past and suggestions for improvement in the future. However, the findings from the studies here will not provide information regarding the accuracy of findings of the included instruments within previous studies where they have been developed or initially used.

WP1 progress and discussion

This WP has progressed slowly but following the recent recruitment of Johan Ohlander (Post-Doc) this will now start in earnest. The WP has moved forward from a strategic perspective, with due consideration being given to how it will be undertaken. For some studies, more than one assessment method has been used. One of the issues to deal with is what level of pesticide exposure do you go to – active ingredient (AI) or pesticide (trade/product name) or broad categories e.g. “herbicide” etc.?

AdB highlighted that project team needs to ensure that WP1 is not referred to as a systematic review as it isn’t. Also need to think about classification of the various study types. The team highlighted that they would be classified in broad categories and it would be good to know, for example, when people started to use algorithms.

AdB advised that in terms of time period for the review that we should pick a time, do the review and then go back another 5 years to see if missed anything.

The AdB highlighted that in terms of timescale for the deliverable it didn’t really matter whether it was completed and delivered in 6 months or a year. Whilst it is good to have a thorough documentation of what has been done it isn’t needed for the other WP to start to move forward.

Progress and discussion on WP2

Qu – do we need to do strict power calculations for each study? If none of them are powerful enough are they still of any use? Agreed that what we are really looking to determine at this stage is sample size.

AdB suggested that the team look at the literature to see if any other studies had a similar aim and identify what the differences are. For example, AB was involved in a study where participants were interviewed a year apart and about a 70% consistency was observed. The team could use this as a data-point to start with and then estimate how many people required to determine if there was, e.g., 20, 30, 40% difference in recall.

Project team highlighted that participants will receive an instrument as close as possible the original questionnaire, delivered using the same methodology where possible so not to introduce any new bias. It is clear, however, that the IMPRESS cannot completely mimic the questionnaires nor procedures previously employed. In some studies the exposure questions are embedded in instruments with questions on many other topics that will not be covered by in IMPRESS. The team had originally considered designing a new questionnaire but decided that this would not be the best approach.

There was some discussions about the length of questionnaires originally used, asking participants to complete questions which aren't relevant to the IMPRESS study (which could be considered unethical) and lead to participant fatigue and, thus, affect results. Action: agreed to remove non-essential questions from the questionnaires to be re-administered so that the questionnaires are focussed on the core questions of interest. It was also highlighted that only asking focussed questions may change the participation rate.

The project team highlighted that Pesticide Users' Health Study (PUHS) questionnaires may not be possible/need to be re-administered to participants of both the PIPAH and PUHS study. This was because consent to link the data from the two studies was needed prior to any use/handling. Action: to seek ethical approval to link the two studies/data sources. Update following meeting and minutes being finalised: Done, ethical approval for this particular aspect has been obtained.

There was some discussion about participants' use of spray records to complete sections of the PIPAH questionnaire and that the participants will simply do this again. This would tell you nothing of their recollection, rather how good they are at copying information from their records. The use of list of pesticides as a means of gaining information for duration and frequency of use was mentioned as an alternative. However, as questionnaires need be reduced in size and provided the use of records mentioned above this is unlikely to be a preferred choice. It was agreed that the project team will look at these particular questions separately from those which recall on actual memory recall.

WP3 discussions

This part of the study will involve the collection of biomonitoring data. In the UK sample collection will be via postal surveys which has been used before. In the other studies, in-situ researchers will assist with the process. The project team highlighted that they are still deliberating this WP3 and are arranging a meeting in Jan/Feb 2018 to discuss this WP in particular in more detail. Some of the questions that they are considering include the validity of one measurement against a questionnaire, if it is better to look at smaller number of people and take lots of samples, rather than vice versa? Also need to consider how this WP links in with WP4 – is it a validation of daily or a more long term exposure as this will require a different sampling strategy.

It was highlighted that different sample strategies may be needed for the different study populations due to differences in pesticide usage. For example, in Ethiopia the same pesticide may be used in multiple applications whereas in the UK it may perhaps only be used in a couple of applications.

Qu – how will we choose what active ingredient to measure? The team responded that we will select those that have a recognised established analytical method, good QA and are extensively used. It is highly likely that the different cohorts will have different AI although the preference would be to have the same active ingredients across all. The use of toxicokinetic models as means of

transforming results to external exposure concentrations (e.g. like in the DEFRA residents study) was also mentioned as an alternative to allow pooling of exposure data for different ingredients.

Underlying aim is to take an algorithm, determine how valid it is for the local conditions under which it is applied. This would determine how exportable this questionnaire is to the other situations. It was highlighted that researchers in British Columbia (Paul Demers (Carex)) may have developed an algorithm and that some Spanish researchers are also doing similar work. Team was encouraged to valuate as many questionnaire as possible, identify what they were developed for and situations where they can and can't be used.

Qu – Had the project team considered hair analysis (for long term exposure assessment)? Response was that it is not considered to be a 'gold standard' which may cause issues when defending the work. The idea was however not discounted but may be considered as an add on if feasible.

Qu – How reliable is the provision of samples via the postal system which has been used in the UK? The response is that it is not possible to answer this and that the project does not have the resources to collect the samples from the UK participants in person. The team did mention that it may be possible to observe a small subset of people but this will be dependent on, e.g. locations, agreement for researchers being on-site etc.

Dissemination activities

The project now has a website which will be populated through the project. Copies of conferences presentations and posters will be included here. At this time the dissemination activities have focussed on introducing the project to stakeholders and the team will be ensuring that sufficient budget is available for dissemination of the results. Both ECPA and the team are committed to disseminating the project via a number of peer-reviewed publications which will be drafted over the project.

Feedback from Advisory Board

It was agreed that the AdB will issue a short report following the meeting summarising their views and advice. It was also indicated that comments to the project documents (e.g. Description of work, protocols etc) by individual members of the AdB will be would be very helpful to the investigators and welcome. Some comments mentioned at the time of the meeting included:

- Careful consideration is needed when looking at available biomonitoring resources and how best to use these to fulfil the study aims and objectives
- Anticipate difficulty in trying to leverage more information from historic studies.
- Why does the sponsor want the study carried out?
- Study will hopefully help improve methods to get better answers scientifically in the future. Need to move away from 'everything in the past is awful'.

Next steps / AOB

Actions:
Minutes to be circulated to project team and AdB for comment. Update following meeting and minutes being finalised: Done
Update PG document in line with requested amendments. Update following meeting and minutes being finalised: Done
Issue COI form for AdB members to sign. Update following meeting and minutes being finalised: Done

Circulate Wp2 protocol and questionnaires to AdB for comment when available

No date as yet has been set for next AdB meeting but it is intended that this will either coincide with a major scientific conference and / or the project team meeting with ECPA.