Incorporation of Dual-Use Considerations into Education Programmes on Responsible Conduct in the Life Sciences: Proof of Concept for a Novel Team-Based Learning System Using a CRISPR/Cas Example

by

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April 2019

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1. Introduction

If there was any remaining doubt, the discovery and application of the simple widely-applicable CRISPR/Cas genome editing technology has demonstrated the urgent need for the whole of the life science community to be aware and well educated about the potential hostile dual-use applications of their work. Yet, almost two decades after this problem began to be clearly recognised in national and international security discussions there is still very limited understanding of the dangers amongst life and associated scientists despite a variety of awareness-raising and educational initiatives that have been taken in different parts of the world.

Building on our own work in this field the paper reports on an attempt to design and test an innovative Team-Based Learning (TBL) system for future largescale educational programmes. This new methodology was tested in a proof of concept experiment using CRISPR/Cas examples to show how it can be used to provide feedback from participants to inform subsequent redesign and test of the TBL in order to achieve specific learning outcomes. The paper begins (Section 2) by introducing the dangers of dual use of CRISPR/Cas genome editing technology and how we had the opportunity to design and run the novel team-based active learning exercise with a group of participants at a workshop on dual use organised by the EU Human Brain Project. In Section 3 we describe how we modified the standard TBL in order to investigate more clearly what participants in the exercise actually learnt about the dangers of dual use and their responsibilities for the societal impact of their work outside of the laboratory, and then in Section 4 we present the results we obtained from carrying out the TBL exercise. This provides the basis for a discussion in Section 5 of why we chose to use certain definitions of dual use and biological security in the TBL, why we chose to use threshold concepts to assess what the participants had gained from the exercise and the ethical difficulties life scientists face in dealing with dual use and
biological security. We conclude in Section 6 that this kind of effective and efficient TBL system could be developed as a core feature of the awareness-raising and education programmes needed to help prevent the future hostile misuse of advances in the life sciences.

2. The Dangers of Dual Use

At an international conference in late November 2018 the Chinese scientist He Jiankui announced that he had made hereditable modifications to human beings using CRISPR/Cas technology. The Chinese scientist maintained that he was proud of his benignly-intended work, but fellow scientists criticised him for what was widely seen as unethical conduct and of bringing the scientific community into disrepute.¹ We agree with both of these criticisms but think that civil society could reasonably ask whether the scientific community could have done more to prevent the unethical conduct in the first place. We think that at least it could have taken effective measures to ensure that the dangers of such misuse were widely understood within the scientific community and therefore have provided reassurance to civil society that it had taken measures to avoid such dangerous research. We illustrate our argument here in regard to the even more dangerous possibility that scientists could deliberately take the results of benignly-intended CRISPR/Cas research and use it for hostile purposes – the vexed question of dual use.

It has been obvious, at least since the early 2000s, that most practicing scientists in relevant fields of civil science have little knowledge of the possibility of dual use of their benignly-intended research² despite many calls for their awareness to be increased.³ However, there has been little research on the structure of the thinking of these scientists and of how their awareness might best be changed so that they appreciate the dangers of dual use and what they might be able to contribute to reducing these dangers. As we can certainly expect many more amazing discoveries in the life and associated sciences in coming decades,⁴ this raises the question of whether there is a more efficient and effective way to
raise the awareness of dual use and promote effective engagement amongst the scientific community so that society can be more prepared for dealing with these issues because scientists are engaged from early on in debates about how important new technologies can best be regulated.

The Advisory Board on Education and Outreach of the Chemical Weapons Convention (CWC) had come to a clear conclusion about what should be done and how it should be done in an important major report in February 2018. In the Board’s opinion the Organisation for the Prohibition of Chemical Weapons (OPCW) which is the international organisation that implements the CWC: 5

“should reach out to new stakeholder communities to raise awareness about their possible contributions to the ‘prevention of the re-emergence of chemical weapons’ and promote professional, scientific, and business cultures that aim to reduce the risks of inadvertently undermining the norm against chemical weapons.”

And it also suggests learning from much research that has been done on how people learn, stating that:

“One of the most important implications of this research is that ‘active learning’ methods, as opposed to traditional, lecture-based instruction in which students are passive recipients, produce better and longer lasting results. The results hold for factual information and for more fundamental concepts. The methods can be applied in many settings, including the classroom, the laboratory, or the field.”

We agreed with these conclusions having been involved in the production of a set of Team-Based Learning (TBL) active exercises on dual use under funding from Canada and the UK
Governments.\textsuperscript{6} TBL exercises clearly have the potential to overcome the well-known difficulty of engaging scientists in the consideration of ethical issues.

We had also been able to run one of these TBL exercises at a meeting organised by the European Union Human Brain Project (HBP) in Stockholm in July 2017 and to report on the success of the exercise in a collection of essays on practical implications of ethics. A video of the exercise was also made available by the Human Brain Project.\textsuperscript{7} As CRISPR/Cas has obvious and major implications for the dual-use of advances in neuroscience\textsuperscript{8} when we were asked to organise another TBL at a second HBP meeting in Stockholm in late 2018\textsuperscript{9} we decided to try to design and test a new TBL system that could help with the long term education programmes needed to change the culture of the life and associated sciences in regard to dual use and biological security using this novel genome editing technology as an example.

3. Design of the TBL

We had three main objectives in carrying out this TBL with a relatively small test group of participants:

1. To design and run a TBL focused on dual-use applications of the novel CRISPR/Cas technology in order to determine the extent that the TBL could be effective in raising the participants’ awareness of the dangers of dual use.

2. To obtain feedback from the participants on the design and running of the TBL in order to develop this TBL for future use.
3. To make an initial attempt to apply a novel approach in a proof of concept experiment that would allow us to gain a better understanding of the participants’ thinking and of how it might be changed more effectively by TBL exercises.

The whole of the meeting in Stockholm was intended to introduce the problem of dual use and all of the participants had given their written consent to taking part in the TBL and for the use of the result of the exercise. When used in full University courses TBL exercises are often carried out in specialised laboratories where each participant uses a computer terminal and the instructor can monitor responses in real time. However, for the kind of largescale dual use education programmes that we think will be needed to change life science communities’ conception of responsible conduct such facilities are unlikely to be widely available. So as has been shown to be effective in numerous setting we did the whole exercise using paper and pencil methods.

In the standard methodology participants are asked to study a small amount of pre-reading directly related to the subject of the TBL. Before they start the exercise, the participants are placed into different teams that sit around separate tables. Then individual participants are asked to complete a questionnaire that has a number of multiple-choice questions related directly to the pre-reading material. This is termed the individual readiness assurance test (iRAT) and after the questionnaire forms have been collected in by the organisers each team is asked to complete the same questionnaire as a team. This is termed the team readiness assurance test (tRAT). After these tRAT questionnaires are collected in and checked the results of the iRATs and the tRATs are relayed back to all participants and discussed by everyone involved in the exercise. It is expected that this mechanism will help to ensure a generally high level of understanding of the pre-reading material and prepare all participants to take part effectively in the following series of (generally) two application
exercises where the groups put their knowledge to use and feedback their conclusions for discussion amongst all of the participants. Following the two application exercises there is also a discussion of the whole exercise by everyone involved. A fundamental point is that the organisers of the exercise have to act as facilitators for the participants to engage in discussions with the subject issue and not as instructors telling them what they should learn. These discussions are also very useful in refining the exercise to make it more interesting and effective, particularly in the first trial runs such as the exercise we describe here. The timings used in the exercise in Stockholm are set out in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Timings for the Stockholm TBL</th>
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<tbody>
<tr>
<td>Introduction: 1:25</td>
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<tr>
<td>iRATs: 1:40</td>
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<tr>
<td>tRATs: 1:50</td>
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<tr>
<td>Marking (of iRATs and tRATs) Break: 2:00</td>
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<td>Feedback and Discussion: 2:20</td>
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<td>Application Exercise 1: 2:30</td>
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<td>Discussion of Application 1: 3:00</td>
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<tr>
<td>Coffee Break: 3:30</td>
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<tr>
<td>Application Exercise 2: 4:00</td>
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<tr>
<td>Discussion of Application Exercise 2: 4:30</td>
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<td>Application Exercise 3*: 5:00</td>
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<td>Roundup Discussion 5:15 – 5:45</td>
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*Participants written comments collected but not discussed.

The participants in the exercise in Stockholm were expected to have quite diverse backgrounds as modern neuroscience draws on many different disciplines. We therefore
carefully constructed the pre-reading in three parts: a simple introduction to CRISPR/Cas technology in a set of power point slides that we had constructed so that everyone had at least a basic knowledge of the technology, and two recent papers which dealt with the societal implications of the use of the technology. The first of these papers dealt with the civil implications of the technology\textsuperscript{10} and the second dealt specifically with the problem of dual use of the technology.\textsuperscript{11} We also suggested that it would be helpful if the participants took a look at the video of the TBL that we had carried in Stockholm in 2017 as this was concerned with the question of dual use more generally. Our participants ranged from postgraduate students through to professional scientists with slightly more men than women taking part. We split the participants into three teams of four people and one team of three people (see Figure 1).

Figure 1: The TBL Teams

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All the participants had received a one-page briefing on the background to our previous work on dual use and TBL exercises so that we could keep the introduction short. In this introduction, we stressed our concern not just with laboratory biosafety and laboratory biosecurity but with security issues well beyond the laboratory door. We defined this concept as Biological Security and presented it in the power point slide shown in Table 2.

<table>
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<th>Table 2: Definition of Biological Security</th>
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<td>Biosecurity and Biosafety (and Biorisk Management) make vital contributions to a wider concept of ‘biological security’ that is made up of a web of integrated and complementary elements that reinforce each other . . . [This] refers to a ‘web of prevention’ that locates biosafety and biosecurity in the context of a range of ‘biological security’ measures that go beyond the laboratory door and include: international and national prohibitions, disease detection and prevention, effective threat preparedness, export controls, oversight of life science activities, and biosecurity education and codes of conduct, the latter ensuring that all those engaged in the life sciences whether in government, industry or academia are aware of their responsibilities to protect their work from misuse to counter the threats to humans, animals, and plants posed by states, non-state actors or other entities.</td>
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As shown in Table 1, this short introduction led straight into the iRATs and tRATs being completed and then into the application exercises.

In a development from the standard methodology in order to help us better understand the impact of the exercise on participants’ appreciation12 of the problem of dual use, before we went into the final discussion at 5:15pm we asked participants if they would individually
take a look at some of the ideas that have been put forward about how concepts might be formed in TBL exercises and write down their reflections on these ideas (Application Exercise 3 in Table 1). We collected in these contributions from participants prior to the final wrap up discussion.

The main question that we wanted to answer was exactly what participants had learned in the exercise and how did that match up to our aim of getting them to understand the profound change that CRISPR/Cas seems to have introduced into concerns about dual-use biotechnology? In Application Exercise 3 we drew on key papers on TBL exercises that have considered what kinds of concepts might be conveyed in learning and teaching in order to attempt to answer that question. According to Shinners-Kennedy\textsuperscript{13}, acquisition by the learner of so-called ‘threshold concepts’ may cause “knowledge integration” transforming the “learners view of their discipline and possibly even their world”. In short, we wanted to know to what extent such a transformation had occurred amongst our participants? Did they now appreciate the very dangerous dual use possibilities opened up by CRISPR/Cas technology and see the need for more effective regulation?

Meyer and Land\textsuperscript{14} have been at the forefront of the threshold concepts debate and whilst numerous methodologies have been designed and deployed in their identification, little or no work research been done carried out on the role of such concepts in the subject area of ‘biological security’ and ‘dual-use’. On the basis of the issues raised in the iRATs/tRATS and in Application Exercises 1 and 2, we sought in Application Exercise 3, to invite the participants to submit reflections which related to ideas put forward by of Meyer and Land. We asked if the TBL changed the way participants viewed ‘responsible science’ (\textit{Transformative}), and if there were concepts that participants found troublesome, counter-intuitive, alien or seemingly incoherent (\textit{Troublesome}). We asked if there were difficult to
unlearn (*Irreversible*) aspects of the TBL and to identify anything that, once learned, was likely, in their view, to bring together different aspects of the subject together (*Integrative*). We asked if the TBL had delineated particular conceptual spaces that served specific and/or a limited purposes (*Bounded*), or if the TBL facilitated enhanced and extended use of language about dual-use and its potential for incorporation into discussion about the subject (*Discursive*). We asked participants if they felt anything discussed / learned during the TBL could be regarded as personally *Reconstitutive*. In other words, we wanted participants to comment whether or not / to what extent their experience of participating in the TBL was likely to be recognised by others? And, whether or not they felt that participation in the TBL may have changed them as individuals and whether or not the experience of the TBL might set them apart from colleagues, and / or influence their professional practice over time (*Reconstitutive*). Finally, we asked participants whether or not they would describe the acquisition of knowledge concerning biological security and dual-use as a transition from A. to B? In other words, whether or not they might liken the experience of the TBL to the crossing of a pedagogic threshold? And / or whether or not they felt that knowledge acquisition in the area of biological security and dual-use involved "...messy journeys back and forth and across conceptual terrain." (*Liminality*).

4. Test of the TBL

The iRATs and tRATs had seven questions and each question suggested four possible answers. These questions related to the power point slides that we had prepared for participants. The questions, however, were deliberately not straightforward: some, for example, asking what was false instead of just asking what was correct (Table 3). In total the responses to the iRAT questions were 80% correct, and as expected, this rose to 90% correct answers for the tRATs as the different groups debated the possibilities. In the discussion
some questions were raised about two of the sets of answers and adjustments have been made to these in order to avoid any ambiguity in future use of the TBL.15

![Table 3: Example of an iRAT/tRAT Question](image)

Application Exercise 1 related specifically to the pre-reading paper by Kang and colleagues and had the following instructions:

“As a Team, discuss each question and agree on an answer to the question. Write your answers on the flipchart provided; and, be prepared to provide clarifications and rationale for selecting your answers.

1. Table 1 [of the paper] represents a ‘summary of genetic correction using CRISPR/Cas9 technology in cell therapy, agriculture, antimicrobials, and anti-viral treatment from 2013 onwards’, in so far as genetic correction has been applied in human, animals and plants. Order this list as a hierarchy indicating, in order of importance, and identify from the list, the ‘genetic correction’ that your Team feel is most ethically, legally and socially problematic.
2. Scientists have identified the technical challenges associated with the development and use of CRISPR technology that ‘hinder it’ from being ‘clinically used.’ Identify three such challenges described by the authors of the above article.

3. ‘CRISPR/Cas9 technology...can be regularly and more efficiently performed in several species of organisms, ranging from insects and plants to rodents and primates.’ According the authors, ‘It can also be carried out in ... stem cells and in human somatic cells for the purposes of basic research’. What challenges and problems arise when considering the use of CRISPR technologies for manipulation of genes in the human germline? What are the benefits and risks?

4. According to the authors this technology has ‘revolutionised genomic research.’ However, they also note that there, ‘remains the risk of improper use’ of this technology. What kind of governance / oversight would be required in order that human germline / embryo gene modification could take place? And what kind of governance / oversight would be required in your view to mitigate the potential for its misuse? “

All four teams produced interesting and detailed answers to these questions on their flipcharts (see Figure 2) and a vigorous debate ensued again with suggestions about how the instructions might be improved.
In Application Exercise 2 we focused directly on the problem of dual use in the paper by Reeves and his colleagues by describing a fictitious scenario and asking teams to decide how to deal with the situation. The exercise instructions were:

“Read the (Scenario) Passage below and agree what the MOST IMPORTANT actions you, as a team of scientists, could take to address the situation described in the scenario. Write your answer on the flipchart. You need to prepare a justification for your answer and be ready to respond to questions and clarification requests from the floor.”
SCENARIO: As an Agricultural Geneticist you know that vertical modification of chromosomes in plant science takes time since modified chromosomes must be vertically inherited from one generation to the next. This can take many growing seasons. However, as a team of scientists working on the development of novel ‘biocontrol’ agents, you come across a technique that facilitates horizontal modification of chromosomes that allows for the editing of crop chromosomes directly in fields. You and your team believe that the regulatory, biological, economic, and societal implications of dispersing such horizontal environmental genetic alteration agents (HEGAAs) into ecosystems are profound. The technique that you have developed in order to disseminate (HEGAAs) in the environment is via insect-based dispersion. Your technique involves a CRISPR system that is engineered to be part of a virus that allows for the modification of plant chromosomes – in other words, this technique would facilitate plant chromosomal editing by means of virally encoded CRISPR proteins that are delivered directly to plants by aphids - that will result in increased plant resilience to environmental challenges and / or herbicides.”

As for the previous exercise the groups had intensive discussions and detailed flip charts were presented and discussed by the teams. The obvious dangers of the work described in the scenario being used to produce a novel biological weapon as suggested in the Reeves paper featured in the presentations and discussions. We then asked for the answers to the questions in Application Exercise 3 to be written down and these answers were collected in. This then led on to a wide-ranging discussion of the exercise in the context of the whole meeting on biological security and dual use in which it seemed that the participants had enjoyed the exercise and found it useful.
The concepts of Meyer and Land and the number of written responses we received from the 14 participants for each were as follows: Transformative (11), Troublesome (12), Irreversible (13), Integrative (12), Bounded (6), Discursive (8), Reconstitutive (9), and Liminal (9). This process therefore resulted in a series of responses that gave intriguing insights into participants experience in taking part in the TBL. However, from our point of view in this exercise it clearly indicated that, while the participants may not have had enough background knowledge of the history of biological weapons and the debates over the last two decades on dual use to fully appreciate the game changing nature of the discovery of CRISPR/Cas technology, there can be little doubt from the responses that participation in the workshop and exercise had an impact on their thinking about the issue (Table 4).

**Table 4 HERE**

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<tr>
<th>Question 1: Transformative</th>
<th>Participants</th>
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<td>Participant 15:</td>
<td>“Responsible science needs to be open and ethical concerns should be integrated into science.”</td>
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<th>Question 2: Troublesome</th>
<th>Participants</th>
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<tr>
<td>Participant 6:</td>
<td>“The possibility/reality that powerful tools like CRISPR/Cas can be used for hostile purposes and maybe not being able to prevent misuse/dual use as a scientist.”</td>
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<tr>
<th>Question 3: Irreversible</th>
<th>Participants</th>
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<tr>
<td>Participant 10:</td>
<td>“CRISPR/Cas as a potent biological weapon and not at all harmless, interesting technology.”</td>
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<tr>
<td>Participant 12:</td>
<td>“The importance of discussing dual use responsible research and innovation.”</td>
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<tr>
<th>Question 4: Integrative</th>
<th>Participants</th>
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Clearly these individual responses to a range of the questions demonstrate that the TBL did have a significant impact on the thinking of participants in the exercise about the question of dual use, particularly as the problems caused by the development of CRISPR/Cas technology as this particular issue had not been given much attention in the workshop outside of the TBL. The answers to Application Exercise 3, however, allow us also to look at the overall impact of the exercise upon the thinking of particular types of people. One answer from a social scientist to all of the questions shows that the questions did not raise any substantially new issues for this participant:
“For me, as a social scientist, all social science concepts discussed today are quite familiar and life science concepts related to CRISPR/Cas9 insects etc. are new but I would not see these life science concepts/terminology as transformative, troublesome in themselves, but I recognise that they raise very important questions about ethical and social implications of science and about responsibility of scientists and others.”

although clearly the importance of the ethical and social implications of scientists’ research and their responsibilities were acknowledged

On the other hand, in the individual answers to the questions from other participants we can observe considerable details about how they responded to the new information made available to them in the TBL. For example, that for some the idea of chemical and biological security has been much broadened:

*Question 6. Identify anything discussed / learned today that, once learned, will allow you to extend (incorporate and enhance) your use of language about this subject (Discursive).*

“For biological/chemical security – much wider/larger than previously thought.”

For others the knowledge about the Chemical Weapons and Biological and Toxin Weapons Conventions has been added to their discursive capabilities:

*Question 6. Identify anything discussed / learned today that, once learned, will allow you to extend (incorporate and enhance) your use of language about this subject (Discursive).*

“Knowledge of e.g. convention about chemical/biological weapons, their implementation.”

The complexity of the dual-use problem also comes through in the individual answers:

*Question 1. What concept discussed / learned today, changes the way you view responsible science (Transformative)? (Transformative)*
“The discussions held about responsible is much more intricate than I thought, coming from someone who only sees the outcome of decisions.”

Thus, the participants were able to recognise and respond interestingly to the categories of questions that we put on the basis of the concepts derived from Meyer and Land.

5. Discussion and Conclusions

The report of a major international meeting of a group of State and NGO experts in 2018 noted that:

“Many participants raised the topic of education and training, with education of scientists as a foundational element for the governance of dual use research. Education was seen as an ongoing activity, not something that happens once and for which researchers will never need additional engagement as science advances. This includes building networks of faculty who can support each other, share best practices, and sustain capacity-building efforts. It requires modules and courses, as well as materials that can be used to teach and engage with scientists about dual use issues. Activities that introduce dual use issues and biosecurity within a wider context, such as the responsible conduct of science, can serve as the basis for more advanced and specialized training.” (emphases added).

In making that Statement the group of experts were reiterating many such statements that have been made by other experts and official bodies since the turn of the century. So clearly one of the key problems in dealing with the whole issue of dual use is the lack of adequate teaching materials that can be efficiently and effectively used to increase the awareness and education of life scientists about this crucial problem.
In relation to the three objectives we had for our TBL, it seems clear that the participants enjoyed and engaged in the exercise over the entire 4-hour period, once again demonstrating that active learning through TBL exercises does help to engage scientists in discussions of dual-use issues. The participants also provided very useful feedback on the iRAT/tRAT questions and the instructions for Application Exercises 1 and 2. Thus, one overall conclusion is that this TBL exercise could easily be repeated in other contexts and would be useful in raising awareness of the problem of potential dual-use applications of this novel CRISPR/Cas technology. However, our main objective was to use the innovation of adding and analysing Application Exercise 3 to make a novel contribution to the larger issue of awareness-raising and education of the whole life and associated scientific communities in the future. As we stated out third objective was:

“To make an initial attempt to apply a novel approach that would allow us to gain a better understanding of the participants’ thinking and of how it might be changed more effectively by TBL exercises.”

Whilst we would not want to take too much from the individual responses in this TBL, it is evident that we have a proof of concept of a novel methodology that allows feedback from the participants in one run of a TBL to be used to modify a subsequent run to refine the materials in order to better achieve the objectives of the exercise. For example, the third Application Exercise could be expanded to investigate aims of the whole TBL by asking the following:

1. Our objectives in this TBL were to communicate the following concepts:
   i. X (e.g., Biological Security)
   ii. Y (e.g., Dual Use)
2. In this Application Exercise 3 we ask for your help in telling us how we might have better communicated these concepts to you so that we can make the TBL more useful for people with your specialist background.

3. In the choice of the background reading.

4. In the introduction to the TBL.

5. In the questions for the iRAT/tRAT.

6. In the feedback on the iRATs/tRATs.

7. In the information for Application Exercise 1.

8. In the discussions on the presentations for Application Exercise 1.

9. In the information for Application Exercise 2.

10. In the discussions on the presentations for Application Exercise 2.

Please be as detailed and critical as you possibly can giving us feedback on what you thought worked well in getting the ideas across and particularly in pointing out what would have worked better for you.

Moreover, this feedback sequence can be repeated several times in TBLs to shape the final TBL for a particular audience in any life science speciality. We think that this approach, with its built-in feedback loop from participants’ response to redesign, would facilitate the much more rapid development of effective TBL exercises with well-defined specific outcomes for particular audiences and thereby simplify the huge problem of awareness-raising and education of scientists in many diverse initiatives that will have to be undertaken rapidly now given the obvious dangers of dual use.

5.1 Definitions

Team-Based Learning exercises take time to design and test, but once this has been done successfully they have proved to be an effective method of conveying key concepts in many educational fields. They are also efficient as they are easily replicated for large groups of people. The designer of a TBL has to work out first what it is intended that participants should take away from the exercise and then to work backwards to produce an exercise to achieve this objective within a standard pedologically-informed methodology. The design
and development of the TBL we have described was based on our views on a number of relevant theoretical issues which we will describe here. The first issue concerns critical definitions used in the TBL. We were particularly interested in making sure that the participants understood the concepts of biological security and dual use, so we took care to make our definitions clear.

**Biological Security**

A confusing and unhelpful characteristic of debate has seen the term ‘biosecurity’ appropriated and applied to discourse developments that take discussion in this area beyond the laboratory door. Indeed, the extended use of this term has to date been a defining feature of much of our own work. On reflection, we feel that this has in some ways has been a source of confusion about this issue, and may have contributed amongst some in the scientific community to a deficit in awareness about the wider notion of ‘biological security’ and of the scope of the problem, and that, an important distinction needs to be made between this term and the association that is suggested by its use with all things within the laboratory. Instead, we suggest that ‘biological security’ better encompasses and covers the range of issues that need to be addressed if effective and efficient risk mitigation and the potential for misuse are to be properly addressed.

Graham Pearson refers to a ‘web of prevention’ that locates biosafety, biosecurity and biorisk management in the context of a range of biological security measures that take our appreciation of biological security beyond the laboratory door. This range of measures include: international and national prohibitions, disease detection and prevention, effective threat preparedness, export controls, oversight of life science activities, codes of conduct, ethics and practice, as well as biosecurity education and awareness raising, the latter ensuring that all those engaged in the life sciences whether in government, industry or academia are
aware of their responsibilities to protect their work from misuse to counter the threats to humans, animals, and plants posed by States, non-State actors or other entities.

Thus, the concept of biological security includes arms control to ban misuse, national legislation to criminalise, oversight of research to ensure good practice, export controls relating to biological materiel to prevent dangerous materiel from getting into the wrong hands, as well as political will to ensure the coherence, efficiency and effectiveness of this wider set of measures in upholding biological security. In other words, if biological security is the overall end, we argue that the specific means to that end include the continual strengthening of what Pearson refers as a web of constraints. This means improving prohibitions, ensuring the effective implementation of legislation and regulatory regimes, monitoring and seeking improvements in responsible conduct of research, good laboratory practice, and keeping a close watch on to whom we transfer materiel and knowledge. This approach both assimilates and incorporates expectations insofar as they relate to reducing and mitigating laboratory risks. However, as can be seen above, biological security takes the debate beyond the laboratory door and inter alia into the realm of concerns relating to national and international security. Thus, the discussion is necessarily extended beyond the confines of safety, security and risk management in the laboratory, and problematically, some may argue, it is taken out of both the comfort zone, as well as out of the specialised areas of interest of professionals working in such fields. Biological security, insofar as we conceive of it, is in our view, best fostered through improvements in awareness of, and though systematic education about, security concerns that include all of the above measures. Thus, we argue that education and awareness through the implementation of deliberative approaches to learning and teaching form an important strand of this overall web of deterrence. However, it is quite clear that this is not widely understood amongst life scientists, so we made sure to emphasis our definition of biological security as described in Section 2 and Table 1.
Dual Use

The awareness and education disconnect from such national and international views identified above is also a characteristic of discussions concerning the notion of dual use. Early in this century problems of risk mitigation and oversight of biological research\(^1\) began to be framed through reports such as the so-called Fink Report,\(^2\) produced under the auspices of the US National Research Council, which identified seven classes of research that would trigger ethical review, and subsequent to that, the so-called Lemon-Relman Report\(^3\) which extended the range of research addressed by Fink to include a wider range of biological problems. Recent attention has focused on so-called ‘gain of function’\(^4\) experiments with attention switching in 2017 - 2018 to address the problem of gene editing. A burgeoning literature thus began to emerge with academic and policy activity taking place across a range of academic sub-disciplines with complex definitions of dual use being put forward and debated. However, this debate can be confusing for those new to the dual-use problem therefore for the purpose of our TBL we thought a simple definition of dual use as “research results that have both civilian and military applications” would be sufficient.

5.2 Threshold Concepts

Emerging from approaches to learning and teaching in field of business management Team-Based-Learning (TBL) is now widely used all over the world across a wide range of academic disciplines.\(^5\) Meyer and Land\(^6\) recognised that certain concepts are often central to the mastery of a subject. Such threshold concepts, as they have become known, are used in curriculum design and in teaching, and are associated with the appreciation of a conceptual approach to understanding. They allow teachers to focus on aspects of curriculum design and teaching that seem central and often difficult to grasp by most learners. Their identification in curriculum design, it is argued, also helps to avoid an “over stuffed” curriculum, and often leads to a “less is more” approach to curriculum design. Since their introduction a decade or
so ago, threshold concepts are increasingly being used to inform curriculum design and to inform the way teachers teach in higher education on a world-wide basis. Threshold concepts are also useful in the design of active and team-based learning (TBL) approaches to curriculum design and teaching. Meyer and Land describe threshold concepts as “akin to a portal, opening up a new and previously inaccessible way of thinking about something….as] a transformed way of understanding, or interpreting, or viewing something without which the learner cannot progress.” Threshold concepts, they argue, have common characteristics in that they are: transformative, troublesome, irreversible, integrative, bounded, discursive, reconstitutive, and liminal. To elaborate regarding the above, according to Barradell, threshold concepts are: (likely to be) transformative, (probably) irreversible, (contain the capacity to be) integrative and bounded, and (be potentially and possibly inherently) troublesome.

Perhaps the biggest problem we have in finding ways to effectively and efficiently helping life and associated scientists through these portals into a wider and effective understanding of their responsibilities is to gain a better understanding of what life scientists think about these issues and how their understanding of responsible conduct might be expanded to incorporate questions of biological security and dual use. That was an important reason why we added Application Exercise 3 to our TBL and used the threshold concepts suggested by Meyer and Land to frame our questions. It is clear that participants understood and were able to respond to the categories proposed by Meyer and Land and that a lot of information can be gained from such responses and the information used to further develop the exercise. However, this approach in our proof of concept exercise should be viewed as a hard case. We used these threshold concepts as they were well based in the TBL literature, but we were far from sure that our participants would respond so readily as they did to the questions in Application Exercise 3. Clearly, as discussed above, in future work it would be
possible to ask a simpler set of questions directly related to the specific concepts that the TBL was designed to convey to participants and to redesign the TBL as necessary for a particular group of specialists to achieve a more effective outcome.

5.3 Ethics

When facing the problem of biological security and dual use practicing life scientists have, at the present time, to deal with issues that they are not often equipped to confront. While these issues are frequently discussed as if they only apply to single experiments within the laboratory, as we have stressed the consequences outside of the laboratory cannot easily be avoided. This line of thinking has perhaps been most thoroughly explored by Frida Kuhlau and her colleagues within the concept of Ethical Competence which:26

“…involves three core capabilities: 1) awareness, to initially recognise an ethically challenging situation; 2) reflection, to ethically reflect on it; and 3) action, to adapt one’s behaviour to it.” (original emphases)

In theory scientists should have been equipped with such ethical competence. Certainly, the current teaching of life scientists about the need for careful consideration of their biosafety and biosecurity within the laboratory has much improved around the world, and that improvement is surely needed for the overall improvement of biological security that we think is necessary given developments such as CRISPR/Cas.

Manifestly, however, life scientists in general do not have such levels of competence to deal with biological security and dual use issues because these also require consideration of potential implications of their work outside of the laboratory and possible activities by others who in the future might have malign intentions. Of course, life scientists do not bear
all of the responsibility for what happens to their work, but we do think that they have some responsibility for helping with the maintenance and development of the international prohibition of chemical and biological weapons. We see a first step in that process is that they become aware of the Chemical Weapons Convention and the Biological and Toxin Weapons Convention and the great difficulty that the international community is having with maintaining and effectively developing these restraints on misuse of benignly-intended scientific research.

6. Conclusion

In conclusion, we suggest that the approach demonstrated here could result in further research and the validation of this novel methodology and thus produce much more effective and efficient awareness raising and education programmes on biosecurity and dual use. This may help to lead eventually to the development of a largescale bottom-up process of empowerment of scientific and civil society actors and their engagement in the management of security issues related to life and associated sciences, contributing significantly to the mitigation of risks deriving from the potential for misuse.


15 The adjusted version of the whole TBL is available on request from Dr. Whitby.


20 The National Academies of Sciences, Engineering and Medicine (2004). *Biotechnology Research in an Age of Terrorism*. Available at: https://www.nap.edu/catalog/10827/biotechnology-research-in-an-age-of-terrorism


