

Prioritisation in the Cancer Network

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1 Introduction

In 2018, the Knowledge Translation (KT) Working Group on Priority Setting published the Cochrane Priority Setting Guidance Note¹. This emphasises the importance of setting systematic review priorities and argues that prioritisation should be embedded into the work of Cochrane Review Groups' (CRGs) to ensure that reviews are relevant to those who use them (e.g. consumers, policy makers, healthcare professionals). Cochrane reviews identified through prioritisation processes that meet the standards outlined in the Priority Setting Guidance Note can be added to the Cochrane Priority Reviews List, updated in real time as reviews are published and new titles added. In the Cancer Network, the National Institute for Health Research (NIHR) Network Support Fellow (NSF) will facilitate this by supporting CRGs with prioritisation activities.

There are six CRGs in the Cancer Network, based in six different countries: Breast Cancer (Australia), Haematological Malignancies (Germany), Childhood Cancer (The Netherlands), Lung Cancer (France), Urology (United States of America) and Gynaecological, Neuro-oncology and Orphan Cancers (United Kingdom). To gain a better understanding of the state of prioritisation in the Network, the NSF held meetings with each Group. The aim was to identify which CRGs have completed prioritisation exercises and which have not, highlight the different priority setting approaches used, discuss CRGs' future prioritisation plans, encourage shared learning between groups and generate ideas about how the NSF can best support CRGs with their prioritisation activities. This report details the information gathered from each meeting, concluding with a Network summary of prioritisation. Appendix 1 contains three tables. Table 1 maps CRGs experience in prioritisation methods. Table 2 aligns CRGs prioritisation exercises with the scenarios from the Cochrane Priority Setting Guidance. Lastly, table 3 shares a good practice example from the Breast Cancer Group of how a prioritisation exercise can be designed to meet the mandatory standards outlined by the KT Working Group on Priority Setting.

1.1 Breast Cancer Group

The Breast Cancer Group is currently conducting their first formal priority setting exercise led by the Managing Editor for the Group, Melina Willson, and their two Co-ordinating Editors: Nicholas Wilcken and Annabel Goodwin. Prior to this, the Group had an informal prioritisation process in place that involved speaking to consumers, oncologists and guideline developers on their editorial board to decide the most important review questions to focus on. They wanted to formalise this process through a prioritisation exercise in which they aim to find the top 10 priority review topics in Breast Cancer, whilst developing relationships with new stakeholders.

The group started their prioritisation work in December 2018 by drafting a prioritisation plan that meets the mandatory standards outlined in the Cochrane Priority Setting Guidance Note. They revisited the plan in February 2019, sending it to their Editorial Board for comment. As per the Group's longstanding policy, they build upon rather than duplicate systematic reviews undertaken by well-established groups in breast cancer, including those of the Early Breast Cancer Trialists' Collaborative Group (EBCTCG, UK). The

EBCTCG conducts individual participant data reviews that are updated in 5-year cycles. Mike Clarke, who is part of the EBCTCG and editor of the Breast Cancer Group, reviewed the prioritisation plan. The Editorial Board approved the plan, the Group published it on their website in May 2019 and circulated it through relevant Cochrane Channels.

The Breast Cancer Group has completed the first step of their plan, analysing Wiley impact data and liaising with their International Editorial Board to develop a preliminary draft list of 25 priority topics in Breast Cancer. They are now embarking on the second step which involves creating a survey. This has raised queries such as which software is the best to use, how much context should be put with each review topic and whether the survey should feature if a topic is open to authors or not. Once the survey is ready, the Group will circulate it to external stakeholders and members of the Cochrane Breast Cancer Group, ask them to add any topics they feel are missing and rank their top 10 priorities. The NSF is working with the Group on their prioritisation exercise, commenting on drafts of their plan and survey, aligning their exercise with the standards from the KT Working Group Priority Setting Guidance (see appendix 1, table 3) and connecting them with UK stakeholders, the UK Breast Cancer Group.

Overall, undertaking this prioritisation exercise has been manageable for the Group alongside their typical workload. They have found it useful to analyse the Wiley impact data for their review portfolio and this has prompted ideas of how they could continue to assess this to influence review updates and set new goals for the group. The process has also helped them to discover external groups they would like to work with more, including some international organisations that are harder to collaborate with due to distance and therefore differing time zones.

This meeting took place on 23rd April 2019 between Eve Tomlinson (Network Support Fellow) and Melina Willson (Managing Editor of the Breast Cancer Review Group).

1.2 Haematological Malignancies Group

The Haematological Malignancies group has not conducted any formal prioritisation of reviews. However, they have recently started thinking about how they can prioritise review updates. They have started to analyse Wiley impact data and have created a spreadsheet of their review portfolio, including information such as number of review citations. They want to add details regarding the guidelines they have been cited in and they plan to get this information from an annual update from Cochrane UK. Whilst in its early stages, the Group have found this an interesting and informative project as prior to this they had not analysed Wiley impact data in such detail. They will continue to develop the survey, add links to guidelines and explore for each review whether evidence is likely to change for reviews due to on going studies.

As well as this work on review updates, the Group are keen to undertake a prioritisation exercise that would result in new titles. They have started to think about the best approach for them, looking to other prioritisation exercises conducted in this area such as the European Haematology Association Prioritisation and the James Lind Alliance (JLA) for Blood Transfusion and Blood Donation for inspiration. The Group recognise that there may be elements of these exercises they could use when developing their own. They have stakeholders in mind that they could work with and are also keen to develop new connections.

This meeting took place on 29th April 2019 between Eve Tomlinson (Network Support Fellow) and the following members of the Haematological Malignancies Review Group: Lise Estcourt (Co-ordinating Editor), Tina Jakob and Vanessa Piechotta (Assistant Managing Editors) and Ina Monsef (Information Specialist).

1.3 Childhood Cancer Group

The Childhood Cancer Group has not conducted prioritisation of reviews. They do not currently prioritise among new reviews or review updates. However, they are interested in completing a prioritisation exercise in the future and wish to explore the potential options for prioritisation of both review updates and new

reviews. Originally they were unsure how they were expected to conduct prioritisation and unclear as to how it would be possible with limited time and resources. However hearing Ruth Foxlee, Senior Advisor to the Editor in Chief, speak at a Cancer Network meeting reassured them that there are many different ways prioritisation of reviews can be done and it does not necessarily have to be very expensive and time consuming. The Childhood Cancer Group has a number of useful connections that would aid them in prioritisation. For example, they have a good relationship with guideline developers both nationally and internationally and as they are based in the Princess Máxima Centre for Paediatric Oncology in Utrecht, they have access to some of the most experienced researchers and paediatric oncologists in Europe. They are keen to hear what other groups are doing and learn from others in the Network.

This meeting took place on 2nd May 2019 between Eve Tomlinson (Network Support Fellow) and Elvira van Dalen (Co-ordinating Editor of the Childhood Cancer Review Group).

1.4 Lung Cancer Group

In October 2017, the Lung Cancer Group completed a priority setting process led by their Managing Editor, Corynne Marchal and the two Co-ordinating Editors: Virginie Westeel and Fergus Macbeth. They decided the focus of the priority reviews should be immunotherapy, came up with review questions in this topic area and submitted them to a commission of experts at the French National Cancer Institute (INCa) to be validated. Following this, they signed a three-year convention with INCa with the aim of answering the priority questions. The Lung Cancer Group has published this process on their website, along with the list of possible titles and on going reviews in the agreed fields. The Group currently has seven titles on the Cochrane priority list.

The Lung Cancer Group completed their priority setting exercise prior to the publication of the Cochrane Priority Setting Guidance. They plan to conduct a new prioritisation exercise in 2019, working with the Cancer NSF to ensure it meets the mandatory/highly desirable standards outlined by the KT Working Group for Priority Setting. They aim to involve the French National Cancer Institute and the French Cooperative Thoracic Intergroup (IFCT) in their prioritisation work.

This meeting took place on 7th May 2019 between Eve Tomlinson (Network Support Fellow), Fergus Macbeth and Virginie Westeel (Co-ordinating Editors of the Lung Cancer Review Group) and Corynne Marchal (Managing Editor of the Lung Cancer Review Group).

1.5 Urology Group

The Urology Group conducted their first formal prioritisation process in 2014, surveying stakeholder representatives of their group to find priority topics in Prostatic Diseases and Urologic Cancer. They included multiple stakeholders in their prioritisation exercise including: the American Urological Association Practice Guidelines Committee, the European Association of Urology Practice Guidelines Committee, the National Cancer Centre Network and the UroEvidence Group for the German Urological Association. The process led to the prioritisation of three review topics, two of which focused on prostatic cancer. All three topics have since been covered in published reviews.

Since 2014, the Urology Group has had an informal process for prioritisation in place. The Group's Co-ordinating Editor, Philipp Dahm, has kept in close contact with stakeholders to ensure that the Group are completing reviews of relevance to end users. The group want to formalise this process with a new prioritisation exercise in 2019. They have started writing a plan and have formed a Priority Setting Steering Group consisting of Juan Franco (Contact Editor), Robert Lane (Managing Editor), Philipp Dahm (Co-ordinating Editor) and Camila Escobar Liquitay (Information Specialist). First, they plan to analyse their current portfolio, classify their reviews (e.g. as new/updated review and what phase they are in) and compare their portfolio with the scope of the group to assess if there are topics within their scope that have not yet been covered. Following this, they will create an online survey and circulate it to relevant stakeholders to generate a list of priority topics, compare these to the current literature and settle on a list

of five priority titles on which editorial resources will then be focused. The Group are keen to begin this process and are optimistic they have the resources to complete it. They also note their interest in learning from other groups' experience in prioritisation and in sharing best practice within the Network.

This meeting took place on 30th May 2019 between Eve Tomlinson (Network Support Fellow), Juan Franco (Contact Editor of the Urology Review Group) and Robert Lane (Managing Editor of the Urology Review Group).

1.6 Gynaecological, Neuro-oncology and Orphan Cancers Group

The Gynaecological, Neuro-oncology and Orphan Cancers (GNOC) group have been involved in five prioritisation exercises over the last 12 years, including in-house exercises, James Lind Alliance Priority Setting Partnerships (JLA PSPs) and prioritisation of review updates.

1.6.1 In-house Prioritisation Exercises

GNOC undertook their first formal prioritisation exercise in 2007, focusing on gynaecological cancer topics as part of a National Institute for Health Research (NIHR) Programme Grant Scheme. This was led by the then Co-ordinating Editor for the Group, Chris Williams, along with four of the Contact Editors as well as the Managing Editors for the group: Clare Jess and Gail Quinn. First, the group emailed stakeholders to introduce the idea of the prioritisation exercise. They outlined their intention to recruit new authors to complete priority reviews who would be trained and supported through the process under the supervision of a Cochrane trained mentor. Stakeholders included Jo's Cervical Cancer Trust and the British Gynaecological Cancer Society as well as an international list of gynaecological cancer clinicians and surgeons. The Group asked them to share their top five priority review topics in gynaecological cancer and collated the feedback, which, once checked for duplication, resulted in a list of 70+ suggested topics. Much like in James Lind Alliance Priority Setting Partnerships (JLA PSP), they then held a meeting with stakeholders at the King's Fund in London, in which they successfully prioritised the top 20 gynaecological cancer reviews and started the process of matching titles with author teams. The funding enabled a 'UK roadshow', which allowed the Group to use a methodologist/statistician to train recruited teams across the country, with email/telephone support also available throughout the three-year grant period. The Group committed to 20 new reviews and 20 updates.

Four years later, in 2011, the Group undertook a similar prioritisation exercise in gynaecological cancer. They emailed stakeholders to ask for priority topics but this time they did not follow this up with a face-to-face meeting. Instead, they created a database of 19 priority topics suggested by stakeholders and circulated this to their Contact Editors for scoring between 1 and 19 (with 1 as the highest priority and 19 as the lowest). The lowest average scoring titles were then selected. These, along with priority updates, led to a list of 25 new reviews and updates completed as part of the second NIHR programme grant. The updates were identified through a plot whereby they collated and used analytic information from Wiley such as the number of citations and downloads reviews had received.

In 2013/2014, the Group conducted their first Neuro-oncology prioritisation process. Robin Grant, Co-ordinating Editor, approached several Neuro-oncology societies to determine their interest in conducting Cochrane reviews. The Group then gave presentations to the interested societies, outlining their ideas for prioritisation and explaining that author training and guidance would be provided in return for authors completing priority review titles in Neuro-oncology. They received interest in completing these reviews from two major Neuro-oncology Societies: the European Association of Neuro-oncology and the Society of Neuro-oncology (USA), who between them funded five top priority reviews under a Cochrane Fellowship Scheme set up by the Group. They used methods similar to those mentioned previously, emailing their editors, stakeholders and authors to ask for priority topics and developing a database of priority topics for their Group Editors to score. The five high priority review titles were then offered to members of the two participating societies. Author teams applied for the topics and their proposals were

circulated to the Group Editors. The Editors then ranked the applications they received and matched the reviews with suitable candidates to start working on the reviews.

1.6.2 James Lind Alliance Priority Setting Partnerships

The GNOC group have been involved in two James Lind Alliance Priority Setting Partnerships (JLA PSP). Information about these can be found online and through the GNOC website, so only a brief outline will be given here. In 2013/2014, the Brain and Spinal Cord Tumour JLA led by Robin Grant took place involving patients, carers, the British Neuro-oncology Society and charities. This JLA produced 10 top priorities in this area and eight were then translated into Cochrane priority review titles. The group are currently working on these as part of the current Cochrane NIHR Programme Grant.

Following this, in 2014-2016, the Womb Cancer Alliance JLA was conducted in collaboration with patients, carers, healthcare professionals and representatives from the Womb Cancer Alliance, the British Gynaecological Cancer Society and GNOC. This JLA led to the production of the top ten priority topics in womb cancer and produced prioritised Cochrane review titles the GNOC group are working on now. A number of the Editorial Team and group consumers were involved in the project.

1.6.3 Prioritisation of Review Updates

The GNOC Group recognise that due to increasing workload and limited resources, it is crucial for them to have a useful and efficient way to prioritise review updates and manage their review portfolio. Therefore, over the past four years they have been organically formulating the best approach for them to prioritise review updates and aid the implementation of the Update Classification System (UCS)². Following on from the work they did in 2010 (see above), the Group began analysing the impact and usage data reports that have been disseminated annually from the Cochrane Library publishers (John Wiley & Sons) since 2009. They produced a tracking system in an Excel spreadsheet, following activity for each review on their portfolio by year using median access scores, Altmetric (AM) score, guideline data, review version, number of included studies and identification of where conclusions have changed. This spreadsheet allowed them to create a list of higher priority updates, which they could circulate to Editors and stakeholders to gauge clinical relevance and inform decisions. They have then used this information to inform the UCS and categorise reviews on the Cochrane Library as 'Up to date', 'Update pending' or 'No update planned'².

The GNOC group note that although they have put a lot of work into developing their strategy for prioritising review updates, it is still a work in progress. For example, they are now going on to think about how they should add weighting to their scores for each category i.e. trying to figure out how they could develop their spreadsheet so that a guideline would carry a heavier weight than a social media reference. The group have found the process extremely helpful as a way of making the best use of group resources, allowing them to focus on the most relevant questions to Cochrane end users. They highlight however that other Groups who want to prioritise review updates may not need to look back as far as they did, as the UCS only requires the use of the past two years of reviews.

Going forward, the GNOC Group aims to continue developing their methods for the prioritisation of review updates. The Cancer NSF will support the Group to write up the process so far and publish this on their website, whilst also helping to write up final reports for the prioritisation exercises they have completed previously. Alongside this, the Group also aim to conduct a new prioritisation process focusing on under-researched areas of gynaecological cancer, such as vulval cancer, to obtain new priority review titles to work on.

This meeting took place on 6th June between Eve Tomlinson (Network Support Fellow), Clare Jess (Managing Editor for the GNOC group), Gail Quinn (Managing Editor for the GNOC group) and Jo Platt (Information Specialist for the GNOC group).

2 Conclusions

This report shows that there is variation across the Cancer Network in the prioritisation processes for reviews. Four out of six CRGs have been involved in formal prioritisation exercises, using different methods ranging from analysing Wiley impact data to prioritise review updates, to using survey-based methods and working with the James Lind Alliance to prioritise new review titles (see appendix 1, table 1). The Gynaecological, Neuro-oncology and Orphan Cancers Group are very experienced in prioritisation, having completed five exercises in the past. The Urology Group has completed a project 5 years ago and is starting another this year. Likewise, the Lung Cancer Group carried out prioritisation in 2017 and aim to complete a further exercise in 2019. The Breast Cancer Group is currently in the midst of their first prioritisation project, working to develop a survey to circulate to stakeholders and consumers (see appendix 1, table 3). Of the other two CRGs, the Haematological Malignancies Group is currently forming ideas on how to approach prioritisation of review updates and the Childhood Cancer Group is keen to undertake a prioritisation exercise but have highlighted that this may be difficult due to a lack of resources to assist the process. Related to this, it is worth noting that as the CRGs in the Cancer Network are based in different countries worldwide, there are differences in the accessibility of grants for funding activities such as prioritisation.

All six CRGs concur that prioritisation is an important exercise to ensure that reviews are relevant to consumers, stakeholders and decision makers. They have all thought about how they could integrate prioritisation with their work (see appendix 1, table 2). Furthermore, the review groups that have recently started working on prioritisation, such as Haematological Malignancies and Breast Cancer, have found it a positive experience and spoken of its benefits e.g. learning about most cited/downloaded reviews via metrics and increasing connections with stakeholders. All CRGs agree that it will be helpful to learn from each other and the NSF will work to encourage shared learning and collaborative working across the Network.

In conclusion, this report gives a useful summary of the current state of prioritisation in the Cancer Network, allowing CRGs to share their experiences, see what others have done and identify who and what they may be able to learn from. It has facilitated the building of connections between the NSF and the individual CRGs and started discussions around how the NSF will be able to support the Groups with prioritisation. For example, some of the suggestions raised include helping the Breast Cancer Group with survey development, working with the Urology Group to develop their plan and align it with the KT mandatory standards and assisting the Gynaecological, Neuro-oncology and Orphan Cancers Group with the writing up of their previous exercises. The NSF will use this report as a base to work from and will continue to liaise with CRGs and the KT Working Group for Priority Setting to establish the best way forward for prioritisation in the Cancer Network.

3 References

¹Cochrane Priority Setting Guidance Note (Version 2). Accessible at: https://training.cochrane.org/sites/training.cochrane.org/files/public/uploads/Partnership_Guidance_May%202018.pdf

² Update Classification System: Guide to Applying to Cochrane Reviews (Version 18 April 2019). Accessible at: https://community.cochrane.org/sites/default/files/uploads/inline-files/Cochrane_UCS-Guide%2018%20April%202019.pdf

4 Appendix 1

4.1.1 Table 1 Experience in Prioritisation Methods in the Six Review Groups.

Cochrane Review Group	Experience in Prioritisation Methods			
	Prioritising review updates (e.g. using the Update Classification System)	Survey to stakeholders/ members	In-house James Lind Alliance	Outsourced James Lind Alliance
Breast Cancer		✓ (Started creating survey June 2019)		
Haematological Malignancies	✓ (Started creating spreadsheet April 2019)			
Childhood Cancer				
Lung Cancer				
Urology		✓		
Gynaecology, Neuro-oncology and Orphan Cancers	✓	✓	✓	✓

4.1.2 Table 2 Aligning the CRGs with the Scenarios outlined in the Knowledge Translation Working Group Guidance Note.

Cochrane Review Group	Scenario	Explanation
Breast Cancer	Scenario 5	They have used Wiley impact data and discussions with their Editorial Board to draft a preliminary list of priority topics and will be circulating this to stakeholders (some global) and consumers to get them to rank it/ add new topics. They currently do not have funding or extra human resources for the project.
Haematological Malignancies	Scenario 2/ Scenario 3	They want to update and prioritise among their existing reviews while allowing additional questions to be added if evidence gaps are identified. They also aim to engage stakeholders and have ideas of new stakeholders to contact. They have limited human resources for the project but are optimistic they will be able to undertake it. They have no financial resources for the project.
Childhood Cancer	Scenario 2/ Scenario 3	They want to update and prioritise among their existing reviews and also conduct prioritisation to find new reviews. They will be able to engage with their current stakeholders and are open to creating new partnerships also. They have limited human resources for the project, as they are a small team with no extra financial resources. It is unclear when they will be able to start prioritisation.
Lung Cancer	Scenario 2/ Scenario 3	The group are still to decide if they wish to prioritise the updating of reviews as well as finding new review titles. They will be able to engage stakeholders they know and are also keen to create new partnerships. They have human resources capable of completing the process in their Group, but no financial resources.
Urology	Scenario 2/ Scenario 3	They want to assess their current portfolio, prioritise their existing reviews and also contact stakeholders (current and new) to generate new priority topics to review. They have human resources capable of completing the process in their Group, but no financial resources.
Gynaecological, Neuro-oncology and Orphan Cancers	Scenario 1/ Scenario 3	They have conducted priority setting exercises in the last five years that require documenting. They are currently prioritising review updates and wish to conduct prioritisation for new titles as well. They have human resources capable of completing the process in their Group, but currently no financial resources for a prioritisation project.

4.1.3 Table 3 An example of how the Breast Cancer Group have met the Mandatory/ Highly Desirable Standards in the Knowledge Translation Working Group Guidance Note.

Name of Cochrane Review Group: Breast Cancer Group		
Category	Standards	Response
Governance	Mandatory: <ul style="list-style-type: none"> Establish a team to lead the priority setting process. As a minimum, this steering group could be drawn from the Group, Network or Field membership. 	<ul style="list-style-type: none"> The team leading the process is drawn from the Group and consists of the managing editor and two coordinating editors.
	Highly Desirable: <ul style="list-style-type: none"> Include stakeholders in the priority setting steering group. 	<ul style="list-style-type: none"> They have not included stakeholders in the priority setting steering group.
Stakeholder Engagement	Mandatory: <ul style="list-style-type: none"> Engage with at least <i>one</i> stakeholder group e.g. guideline developer, funder, consumer organisation, professional society etc. This must extend beyond the Group, Network or Field membership and/or editorial boards. Publish, through relevant Cochrane channels, the intention to conduct prioritisation, to give external and internal stakeholders (Groups, Networks and Fields) an opportunity to be involved (e.g. by facilitating connections to external stakeholders in other geographic areas, or in a specific thematic area). 	<ul style="list-style-type: none"> The Group have engaged with external stakeholder groups (“advocacy groups, clinical specialities, medical colleges etc” and members subscribed to the newsletter). The plan has been published on the Group website and through Cochrane channels.
	Highly Desirable: <ul style="list-style-type: none"> Engagement with <i>multiple</i> stakeholder groups. 	<ul style="list-style-type: none"> The Group have engaged with multiple stakeholder groups (advocacy groups, clinical specialities, medical colleges etc and members subscribed to the newsletter).
Documentation and Dissemination	Mandatory: <ul style="list-style-type: none"> Document the priority setting plan, detailing stakeholder engagement, methods and criteria that will be used for the priority setting process. Document the implementation of the prioritisation process and make it available online on the Group, Network or Field website. CRGs should include a link to the Network portal. Publish list of priority topics (in the form of new or existing review titles or 	<ul style="list-style-type: none"> The group have documented the priority setting plan. N/A at this point, but they plan to do this N/A at this point, but they plan to do this N/A at this point, but they plan to do this N/A at this point, but they plan to do this

	<p>placeholder titles where the precise question is yet to be determined) on individual, group or field website.</p> <ul style="list-style-type: none"> • Ensure priority reviews are promoted on publication using the KT dissemination brief. • Provide formal feedback on the results of the priority setting process to the stakeholders that were involved in it. 	
	<p>Highly Desirable:</p> <ul style="list-style-type: none"> • Publish a more detailed report of the prioritisation process in a relevant academic journal • Publish a more detailed report of the prioritisation process on the individual Group, Network or Field Website. • Notify Stakeholders when the priority reviews have been conducted. • Develop a plan for how priority reviews will be delivered. • Evaluate the prioritisation process and outcomes. 	<ul style="list-style-type: none"> • Not planned as yet
<p>Currency/ Timeframe</p>	<p>Mandatory:</p> <ul style="list-style-type: none"> • The prioritisation process should be repeated at regular intervals, according to emerging treatment and intervention options within the Group, Network or Field scope and changing stakeholder needs. At a minimum, every 5 years. 	<ul style="list-style-type: none"> • Annually the Group will scan citation metrics from Wiley and consider adding/revising priority topics based on that and other important external feedback (e.g. hot topics at San Antonio Breast Cancer Symposium). • Every three years they will consider repeating this priority exercise.
	<p>Highly Desirable:</p> <ul style="list-style-type: none"> • The prioritisation process should be current i.e. repeated within 3 years. 	<ul style="list-style-type: none"> • The Group are going to consider repeating the process every three years.