FINAL

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MINUTES OF THE NINTH DEPLETED URANIUM SCREENING PROGRAMME OVERSIGHT BOARD MEETING ON 11th MARCH 2003

Present:			
Board:	Professor David Coggon	MRC	Chair
	Surg. Cdre Nick Baldock	INM	
	Mr Ron Brown	DRPS	
	Dr Chris Busby	LLRC	
	Mr Ivor Connolly	NGV&FA	
	Dr George Etherington *representing Miss Frances Fry*	NRPB	
	Mr Jim Glennon	NGV&FA	
	Dr Muir Gray	NSC	
	Miss Beverley Green	RBL	
	Professor Malcolm Hooper	GVA	
	Dr David Lewis	INM	
	Dr Gordon Paterson	BRC	
	Professor Brian Spratt	RS	
	GVIU Representative	GVIU	Secretary
Observers:	Air Cdre Simon Dougherty	DMSD	
	Mr Neville Higham	HSE	
	Mrs Brigid Rodgers	GVIU	
	Miss Rosie Wane	GVIU	
	Mrs Janie Walker	GVIU	
	Wg Cdr Charlie Wilcock	DMSD	
Guest:	Gideon Henderson	OU	
Apologies:	Mr Alan Duncan	HJA	
	Miss Frances Fry	NRPB	
	Professor Ian Gilmore	RBL	
	Dr Len Levy	MRC IEH	
	Dr Margaret Spittle	MH	
	Dr Hilary Walker	DH	

Item	Discussion and Decisions	Actions (Action date)
1.	**Introduction** a) The Chairman welcomed board members to the meeting. b) George Etherington stated that Frances Fry was taking early retirement and would no longer be attending the DUOB. Dr Etherington had represented the NRPB on a number of occasions in Frances's absence and NRPB were happy for him to be their representative on the DUOB. This was agreed by Board members. **Action 9.1. The Secretary undertook to seek approval from US of S for George Etherington's appointment to the DUOB.** c) The Chairman stated that Peter van Calsteren had resigned from the DUOB due to a potential conflict of interests. Dr van Calsteren had asked for this issue to be discussed at this meeting. The DUOB agreed that it had been appropriate for Dr van Calsteren to resign from the Board in the circumstances. d) As a result of Dr. van Calsteren's resignation, there was a need to fill a gap in expertise on the OB. At the Chairman's suggestion, Dr. Gideon Henderson from Oxford University had therefore been invited to attend this meeting as a guest and possible future member of the Board. Dr Henderson introduced himself as a lecturer in environmental earth sciences at University College, Oxford. Dr Henderson pointed out that his department had links with Professor Sir Keith O'Nions, the Chief Scientific Advisor (CSA) to the MOD. Dr Henderson stated that CSA was a previous head of the Department of Earth Sciences and still had a nominal role in the department. Dr Henderson had worked with CSA in the past and had not bid for the main testing contract because of this link. Jim Glennon asked if his department received any funding from the MOD. Dr Henderson stated that he was unaware of any MOD funding within his department and undertook to check this fact. He also undertook to provide details of his background. A decision regarding Dr Henderson's membership of the DUOB would be taken outside of the meeting. e) Chris Busby spoke briefly about a proposal he wished to bring to the table regarding the recent deployment of troops to the Gulf. As this was not within the Terms of Reference of the DUOB, it was agreed to discuss it later under A.O.B. f) The Chairman noted that the Secretary had been drafting various documents for the DUOB, but it was important that all members of the Board contribute to the process by commenting on the drafts in timely fashion. At present, comments on documents were generally received from only a core of 3 or 4 members. He asked that if a Board member had no comments on a document then an email to this effect should be sent to the Secretary within the required timescale.	Secretary (28/3/03)
2.	**Minutes of Last Meeting** a) Minor changes to the minutes of the last meeting were agreed by all Board members. **Action 9.2. Secretary to amend minutes of 8th DUOB and circulate** b) Jim Glennon queried the meaning of paragraph 8e in the last minutes. It was	Secretary (12/3/03)

	agreed that this paragraph was clear in that if a veteran requested a re-test this would have to be considered on its individual merits. Gordon Paterson suggested it would be wise to check the NHS situation. He stated that while an NHS patient is entitled to a second opinion he was unsure if this extended to a repeat of a laboratory test. **Action 9.3. Gordon Paterson to supply details on NHS re-test policy**	Paterson (4/4/03)
3.	**Matters arising from last meeting** Documents a) The Secretary confirmed he had distributed the following documents: • Final minutes of 7th meeting • Malcolm Hooper's email regarding the DU questionnaire • Final SOR for extended pilot exercise • Target isotope ratios for the extended pilot study (to a subset of the DUOB) • Schedule for putting the screening programme in place Questionnaire to people having a test b) Malcolm Hooper had received comments from the Chairman and Ron Brown. The questionnaire is discussed in section 8 of these minutes. Summary of pilot exercise c) The Secretary stated that he had completed this action and the summary was available on the DUOB website. Thymol d) Brian Spratt had received advice from two sources indicatingthat there was no need to add thymol to urine other than in exceptional circumstances. It was agreed therefore that there was no need for the DUOB SORs to specify that thymol be added to urine samples. Contracted laboratories would be responsible for the health and safety aspects of dealing with the samples. SOR for Main Contract e) The Secretary stated that he was working on the next draft of the SOR for the main contract for laboratory testing which would be circulated soon. He stressed that some of this work was outside his area of expertise and he needed as much help from Board members as possible. Plan for Analysis of Pilot Study results f) The Chairman had produced a draft plan for examining the pilot study results. This is discussed under section 7. Information for GPs etc. g) The Chairman had produced new drafts of the information. This is discussed under section 9. DU Research h) With regard to section 7b of the last minutes, the Chairman stated that he had attended a meeting of the MRC Military Health Research Advisory Group	

	(MHRAG) (a committee established to advise the MOD) at the end of January. DU had been discussed at the meeting – the general view was that this subject was not a research priority. The Chairman said that he had pointed out that it was a priority for some veterans. Chris Busby expressed concern that if the MRC was saying that DU research was not a priority then funding would not be available for related epidemiological studies. The Secretary pointed out that the MOD had stated that it would fund epidemiological studies once the screening programme had been set up. The Chairman said that in relation to this research, the MRC would not be asked to comment on the priority of proposed studies, but on their validity. i) Ivor Connolly stated that, in his view, research tended to look at a subject in isolation and did not study the combined effects of a number of factors. The Chairman said that he believed that Porton Down research was looking at interactions between vaccines and NAPS. He suggested that if members had reasons to suspect a toxic interaction between DU and other exposures in the Gulf or Balkans, they could present their ideas to a future meeting of the Board. Post meeting note: The Vaccines Interactions Research Programme will complete in December 2003	
4.	**<u>Update on Extended Pilot Exercise</u>** a) The laboratory responsible for producing the spiking solution for the pilot study had written a detailed report on this. Dr. Henderson stated that from a brief look at the report the work appeared to have been done very carefully and along sensible lines. Dr. Henderson expressed concern over two issues. He asked if the fact that uranium could be diet dependent had been taken into consideration. The Chairman replied that the uranium content and isotope ratios of the unspiked urine samples would be checked. Dr. Henderson also expressed concern over the laboratory's ability accurately to measure a zero U236 reading. Dr. Henderson undertook to have a more detailed read of the paper and report back to the DUOB. **<u>Action 9.4. Dr Gideon Henderson to report back to DUOB on the spiking solution paper</u>** Post meeting note: Dr. Henderson emailed the Secretary on 13th March stating that the U236 issue appeared to have been dealt with satisfactorily. b) The Chairman commented that the report indicated that the spiking samples had been produced correctly and that the go-ahead had been given for the laboratory to distribute the spiking solution to the other laboratories. The Secretary stated that he expected this to happen by the end of the week. Post meeting note: The spiking solution was delivered to the laboratories on 10/3/03. c) Chris Busby asked about the problem of uranium absorption in the containers. David Lewis stated he had carried out experiments in his laboratory which indicated that this was not a problem in polyethylene bottles if the urine was acidified. d) It had originally been intended that, once the three laboratories had produced the spiked samples, they would be sent to Peter van Calsteren's laboratory, where they would be re-labelled and distributed back to the other laboratories for measurement. It was agreed that it would not be appropriate for Dr van Calsteren to carry out this task following his resignation, and Gideon Henderson was asked if there was a possibility of carrying out the task at his	Henderson (21/3/03)

	laboratory. Dr Henderson stated that he saw no problem with this but needed to check a few details before he could commit to it. Post meeting note: Dr Henderson confirmed by email on 13/3 that it would be possible to re-label the samples at his laboratory. **Action 9.5. Secretary to arrange the re-labelling exercise with the relevant parties.** e) Gideon Henderson asked if all the laboratories were using the same containers for the final spiked samples. The Secretary confirmed that this was specified in the contract and had been brought up in discussions with the 3 laboratories. He undertook to check this. Gideon Henderson also stated that it was necessary to check how the laboratories intended to label the containers. The Secretary also agreed to check this. **Action 9.6. Secretary to check on sample containers** **Action 9.7 Secretary to check on sample labels** Analysis of pilot study results f) The Chairman had produced a short plan of how the pilot exercise results could be analysed (Attached at Annex A). He talked through this paper, stating that Item 7 (checking that discrepancies between laboratories and in comparison to expected values are within the quoted ranges of error for each laboratory) would probably be the most difficult for him. The DUOB were asked to comment on this paper within two weeks. **Action 9.8. DUOB members to comment on analysis of pilot exercise results**	Secretary (28/3/03) Secretary (28/3/03) Secretary (28/3/03) All (28/3/03)
5.	**Draft SOR for Normative Value Study** a) This SOR had been distributed prior to the meeting but did not include comments received since that time. The Chairman stated that there were 4 main reasons for the normative value study: • To establish the range of urinary uranium excretion and isotope ratios in the general population • To explore potential determinants of variation between individuals such as place of residence and occupation • To examine how uranium excretion varies throughout the day • To establish how repeatable results are from one day to another b) A number of issues were discussed, particularly with regard to factors that might be associated with variation in uranium excretion. These included: • Age • Sex • Residence near to the coast • Residence near to nuclear facilities etc. c) The Chairman undertook to produce the next draft of the Statement of Requirement. **Action 9.9. Chairman to produce fourth draft of Statement of Requirement for Normative Value Study.** d) The Secretary stated that this was a small contract and did not need to be advertised. A contractor had been suggested for this study at a previous	Chairman (21/3/03)

	meeting. The Secretary stated that he had been in preliminary discussions with this organisation.	
6.	**<u>Draft Advertisement for Health Provider Contract</u>** a) The Secretary stated that the activities leading up to placing the Health Provider Contract now formed the critical path for the screening programme. This advertisement needed to be placed as soon as possible to ensure that no further delay occurred in the programme. [There had been no point in advertising this previously as Invitations To Tender for the Health Provider Contract would be issued in parallel to the main testing contract once it was established that a suitable test was available]. b) Minor alterations to the advertisement were agreed. Post meeting note: The revised advert was circulated by email following this meeting and a few minor comments received. The final version was sent to MOD Contracts Branch on 14/3/03.	
7.	**<u>Main Testing Contract</u>** a) The Chairman sought to clarify a number of issues with regard to the main testing contract. <u>Number of Laboratories for Main testing Contract</u> b) It was agreed that, if possible, 3 laboratories should be involved in the main testing programme as this provided scope for interlaboratory comparison and also provided back-up if one of the laboratories dropped out. c) Ivor Connolly asked why the main testing contract had been advertised to laboratories other than those taking part in the current pilot exercise as this seemed to be delaying the programme. The Chairman explained that, because of the uncertainty over the existence of a suitable test, the initial requirement had been advertised for a pilot study to examine a number of techniques. There would have been no point placing a contract for the main testing programme at that stage. Because of the value of the main testing contract, European Union rules required that the main testing contract be advertised in the Official Journal of the European Community. This had elicited 7 expressions of interest in carrying out the main testing contract. However many laboratories were asked to tender for the contract, these would all have a set time to answer the ITT and would be considered at the same time. Hence there would be no additional delay to the programme from inclusion of laboratories other than those carrying out the pilot study. <u>Treatment of Sample</u> d) It was agreed that the laboratories involved in the main testing programme would be responsible for organising the measurement of creatinine. It was also agreed that acidification of urine samples should take place in the laboratories rather than at the point of collection. No decision was reached on whether the samples needed to be refrigerated. David Lewis undertook to advise on these issues. Post meeting note: The SOR for the Health Provider Contract will specify that the samples must be delivered to the laboratories within 5 days of sample collection. Consideration of creatinine measurements, acidification and refrigeration must be made with this period in mind.	

	Action 9.10. David Lewis to advise on creatinine measurements, acidification and refrigeration of samples Splitting of Samples e) It was agreed that there was no need to split the samples for security purposes. If a repeat test was required, the veteran could provide a second sample. f) Samples might, however, need to be split for the purpose of Quality Control, with analysis of the same sample by two or more laboratories. Quality Control g) Quality Control would be achieved by analysing some of the samples in duplicate and by providing spiked samples as in the pilot exercise. h) It was agreed that once contracts were let for the main testing programme it would be a good idea to get the contracted laboratories together to discuss how a Quality Control programme could be carried out. Assessment of Expressions of Interest in Main Testing Contract i) The Secretary reminded the Board that the main testing programme had been advertised last year, prior to the results from the first pilot study. Seven organisations had expressed an interest in bidding for the main testing contract. The Secretary stated that he now wanted expert input on which organisations should be invited to tender. Gideon Henderson and David Lewis were tasked with looking at the Expressions of Interest, and advising on this. **Action 9.11. Gideon Henderson and David Lewis to review the expressions of interest for the main testing contract**	Lewis (28/3/03) Henderson/ Lewis (21/3/03)
8.	**Questionnaire** a) A revised draft of the questionnaire by Malcolm Hooper had been distributed to the DUOB prior to this meeting. There was considerable discussion about the purpose of the questionnaire, particularly with regard to whether and how it should be used for research purposes. Beverley Green pointed out that it had previously been agreed by the DUOB that the questionnaire would be used primarily for clinical purposes and not to generate data for research. Chris Busby argued that any data obtained could be used for hypotheses generation. The Chairman stated that data linking DU exposure to health were likely to be biased as the scheme was voluntary. This would make meaningful interpretation virtually impossible. b) There was a great deal of discussion about whether a question should be included asking if the veteran had cancer. The Chairman argued that an open question asking about any illnesses that the veteran was worried about would be more useful for clinical purposes. Beverley Green stated that under the Data Protection Act it was necessary to have a reason for collecting specific data i.e. it is not allowed to ask for information without having a specific purpose for those data. c) Gordon Paterson pointed out that the Factsheet supplied to the veteran would detail the alleged health risks of DU and most likely promptthe veteran to consider cancers etc. in answering an open question. Chris Busby argued that an open question would not generate information on where the cancers	

	appeared. Brian Spratt asked if this was something that could be picked up when the veteran visited the Health Provider and handed in the questionnaire. David Lewis asked if a cancer question could be considered leading and might generate unnecessary fear. d) Chris Busby asked for a vote on whether an explicit question about whether the veteran had cancer should be included. Four people voted for the question and seven voted against with one abstention. It was therefore agreed that the cancer question would not be included in the questionnaire e) There were further comments on the questionnaire as follows: • The question about alcohol consumption should be removed – but smoking left in • Acronyms should be expressed in full • The occupation of the veteran should be considered carefully as many service personnel perform tasks outside of their designated role • The layout of the questionnaire must be further considered • Possible inclusion of earlier residential history f) Beverley Green expressed the view that the question relating to satisfaction with the MOD Medical Assessment Programme was not relevant. Malcolm Hooper explained that he was trying to collect evidence that would support or disprove the feeling among veterans of his acquaintance that the published figure of 95% satisfaction with the MAP was incorrect. Post meeting note: The MAP satisfaction questionnaire is given to the veteran at the beginning of the visit and generally filled out while the veteran is waiting for blood tests etc. At no point does a member of the MAP staff sit with the veteran or prompt answers. The anonymous questionnaire is placed into a box when the veteran leaves and the forms are examined and the statistics updated approximately every two months.	
9.	**Information to Veterans/GPs** a) Muir Gray stated that he had done some work regarding the information that should be supplied to veterans and their GPs. He distributed the papers attached at Annex B. b) Muir Gray recommended that the advice to veterans and GPs be combined into a single piece of information. c) Muir Gray also recommended that the work produced on this so far should be passed to an organisation with experience in the preparation of resources for clinicians and 'patients'. His paper briefly discussed three organisations that could carry out the task. The chosen organisation would take the information that had already been produced, develop it using focus groups and then supply the tested resources. The DUOB agreed with this approach and Muir Gray undertook to prepare a report based on his discussions with the three organisations. **Action 9.12. Muir Gray to produce report on his discussion with the three organisations.** d) Muir Gray suggested that two members of the DUOB should be nominated to help with the production of the information. Muir Gray and Gordon Paterson were nominated by the Board	Gray (28/3/03)

10.	**Timescales** a) The Secretary pointed out that the schedule for implementing the screening programme was very tight, particularly with regard to the Health Provider Contract. He also pointed out that if the next meeting was scheduled for May then the SORs for the three contracts (main testing programme, Health Provider and normative value study would need to be discussed and agreed ex-committee. He again stressed that he would need the Board's co-operation to achieve this.	
11.	**DU Background and Scientific Issues** a) David Lewis had recently visited a number of organisations in the US on behalf of the Chairman. He provided a brief of his activities in the US, attached at Annex C.	
12.	**Date of next meeting** a) The date for the next meeting was set for 12th May 2003.	
13.	**A.O.B.** a) Malcolm Hooper presented a proposal by Chris Busby (who had to leave the meeting early). The main points of the proposal were that: 1) British soldiers engaged in operations in southern Iraq should be given respirators or masks capable of stopping particles down to 0.1 microns. 2) British soldiers should be adequately and fully warned of the dangers from DU particles 3) That British Forces should be made aware that following any conflict they could ask for urine tests and be included in the testing programme being carried out under the direction of the DUOB b) The Chairman pointed out that points 1 and 2 were outside the terms of reference of the DUOB. However, Brigid Rodgers gave a brief summary of the instructions that have been given to British troops: • General health and safety instructions for UK troops, which cover encounters with DU, are incorporated in the Mounting Instructions for the operation which have been passed to the units involved • Safety instructions, covering all aspects of the hazard management of DU munitions in theatre, have also been issued by the Permanent Joint Headquarters (PJHQ) through the operational chain of command to all units and formations deployed in the Joint Area of Operations • Specific instructions and training packages exist for Explosive Ordnance Disposal (EOD), Royal Armoured Corps (RAC) and support personnel, those most likely to come into contact with DU munitions or dust. Radiation monitoring equipment has also been provided to some EOD units. Brigid Rodgers stated that these safety instructions would soon be made available to the members of the DUOB c) With regard to point 3 of Chris Busby's proposal Brigid Rodgers pointed out that the MOD Biological Monitoring policy (www.mod.uk/Defence Issues/Health and Safety/Depleted Uranium) had been discussed at the last DUOB meeting. Under this policy post-deployment monitoring would take place on return from the area of operations. Levels 1 and 2, according to the	

	definitions used by the Royal Society, would be encouraged to receive testing and Level 3 (which includes all personnel who have operated in a theatre where DU has been used) would be offered a test on a voluntary basis. These personnel would be tested with a less sensitive assay than that being explored by the DUOB to assess exposures after an interval of up to 13 years. d) In addition to this Brigid Rodgers provided further information about a suggestion made at the last DUOB meeting regarding pre-deployment testing of troops heading to the Gulf area. This would not be carried out for a number of reasons (discussed at the last meeting). However, a normative value study of military personnel was being planned – this would be carried out in addition to the normative value study of the general population being planned by the DUOB. The subjects of the study would be military personnel in the UK and Germany and would be representative of those currently deployed to the Gulf area. e) Charlie Wilcock (Defence Medical Services Department) reiterated that all those deployed to the Gulf would be eligible for a post-deployment test should DU be used. Returning troops would be given an information card stating that DU had been used and how to apply for a test. He also explained that it was considered impractical to take samples from those already deployed in the region due to the activities being carried out. Also the DU pilot exercise had already demonstrated the ease with which contamination of samples can occur and this would be a much worse problem in the middle of the desert. f) Gordon Paterson expressed the view that, from an epidemiological point of view the normative value study appeared to be sound and that it was not necessary for pre- and post-deployment testing to be carried out on the same personnel. Malcolm Hooper reiterated his view that the biological half-life of soluble uranium was 36 hours and that by the time personnel returned from the Gulf the uranium in their bodies would be much reduced. Ron Brown stated that he had seen no evidence of this timescale and asked Malcolm Hooper to provide his source of information about this. Brain Spratt stated that he was confident that DU would be easily detectable for up to a year following exposure. **Action 9.13. Malcolm Hooper to provide information regarding biological half-life of soluble uranium.** g) Ivor Connolly expressed the view that the DUOB should recommend to the MOD what tests should be carried out in the Gulf and when the troops returned home. The Chairman pointed out that this was outside the terms of reference for the DUOB. Post meeting note: As the subject of the terms of reference of the DUOB was mentioned a number of time during this meeting, a copy of the TOR is attached at Annex D	Hooper (28/3/03)

Distribution:

All members

All observers

Devolved Health Administrations

Annex A -Plan of Analysis for Extension to Pilot Exercise

1. Compare results for spiking solution – between laboratories and with expected values.

2. Determine best estimate for uranium concentration and isotope ratios of spiking solution.

3. Compare results for unspiked urines – between laboratories, and within laboratories according to sample size.

4. Determine best estimates for uranium concentration, isotope ratios, and "concentrations" of natural and depleted uranium in the three unspiked samples of urine. (n.b. we do not expect to find any evidence of depleted or enriched uranium in these samples.)

5. Compare results (total uranium concentration, isotope ratios, and "concentrations" of natural and depleted uranium) for spiked urines – between laboratories, within laboratories according to sample size, and with expected values based on the best estimates determined previously for the spiking solution and unspiked urines.

6. For each laboratory and sample size, compare the results for spiked samples with those expected from the unspiked sample and the composition of spiking solution as measured by that laboratory.

7. Check whether the discrepancies between laboratories and in comparison with expected values are within the quoted ranges of error for each laboratory.

ANNEX B

OUTPUTS-BASED SPECIFICATION FOR THE PREPARATION OF PUBLIC AND PROFESSIONAL INFORMATION ABOUT TESTING FOR DEPLETED URANIUM

The National Screening Committee wishes to commission, on behalf of the Depleted Uranium Oversight Board, the appraisal of draft information sheets for clinicians and patients. The outputs that would be expected from the project would be:

- a general practitioner information sheet which had been tested with focus groups of general practitioners for readability and usefulness; the general practitioners would also be asked how much of the information being given to people being tested they wished to see;

- a question and answer sheet for those offered the test which had been piloted and evaluated with a focus group of veterans; it would be assumed that this would be made available for two levels of readability using a standard process for assessing readability;

- a report describing the process that had been undertaken in the preparation of these resources, together with any additional recommendations the team carrying out the development project wished to make.

Time scale

The time scale would be determined by the Ministry of Defence but testing should not start until the Depleted Uranium Oversight Board was satisfied that they had valid and useful resources for both clinicians and patients to accompany the testing process.

J A Muir Gray, CBE, DSc, MD, FRCP, FRCPSGlas
Programme Director – UK National Screening Committee

DEVELOPMENT OF INFORMATION SHEETS FOR CLINICIANS AND VETERANS

Background

The National Screening Committee undertook to help the DUOB with the quality assurance of information prepared for clinicians and veterans because of their experience in developing resources to ensure that people offered tests made an informed choice about whether or not they accepted the test.

A draft letter to general practitioners has been prepared with a depleted uranium fact sheet. In addition a question and answer sheet has been prepared for those seeking a test for depleted uranium.

The issues

In preparing material of this sort there are a number of issues that need to be considered. Two that are of particular importance are:

1. Should there be material specifically written for clinicians and for members of the public, or should the same material be available to all with members of the public also having access to the same content in a simpler style? At present the proposal is that general practitioners receive a fact sheet with those who are seeking a test for depleted uranium being offered a question and answer sheet. Some healthcare professionals prefer question and answer as a means of assimilating unfamiliar knowledge and some healthcare professionals would probably prefer the question and answer format although this does not cover all of the issues covered by the fact sheet.

2. Similarly there are some facts on the fact sheet which are not contained in the question and answer sheet and some people offered testing would probably like this fact sheet linked to the question and answer sheet. It is also possible that some veterans will want more information than healthcare professionals are offered because exposure to depleted uranium is perceived by them as a risk of very high significance, whereas the healthcare professional, particularly if he or she does not understand all the issues involved, may not see it as such a serious issue.

Testing of the draft materials

It is proposed that the services of a centre with the tools, experience and credibility in the preparation of resources for clinicians and patients be obtained to test the resources that have been prepared and address the two questions set out above. This would be done by developing focus groups of veterans and clinicians and discussing with them both the questions raised above and any questions that may be raised by the DUOB, and then appraising the individual documents.

Document appraisal will be carried out using standardised techniques such as the DISCERN instrument. This has been validated as a means of appraising patient

information and covers not only the clarity of the English but also the strength of the evidence base. Furthermore, the people who carry out this appraisal have experience of developing patient information materials for a range of groups and could advise on the need for one level or more than one level of resource to be made available.

The process of procurement

Three organisations have been invited to express an interest in carrying out this work. They are widely regarded as the leaders in the field both nationally and internationally and are independent organisations. All organisations have received grants from the Department of Health in the past but they are charities and would certainly not see themselves as part of government. All three have a mission to ensure that patients and members of the public are adequately informed about the choices they face.

Using the specification attached as an appendix, one of the three organisations described briefly below will be asked to carry out the work.

It is recommended that the DUOB nominate two people to help in the selection process and sit on a small project board that could be consulted during the course of the project if necessary.

[Information on individual organisations removed – Secretary]

Annex C – David Lewis Brief on US Visit

DEPLETED URANIUM ANALYSIS CAPABILITY IN THE USA.

1. **Introduction.**

1.1 MOD members visited the USA between 24th and 26th February to discuss issues surrounding depleted uranium exposure in US Gulf war veterans. This included visits to a number of US Armed Forces establishments where depleted uranium (DU) analysis was being performed and offered the opportunity to discuss analytical methods and instrumentation.

1.2 The following establishments were visited.

- The Armed Forces Radiobiology Research Institute (AFRRI)
- The Armed Forces Institute of Pathology (AFIP)
- The US Army Centre for Health Promotion and Preventive Medicine (CHPPM)
- The Veterans Assessment Medical Centre Baltimore (VAMC)

2. **AFRRI**

2.1 AFFRI is responsible for medical nuclear and radiological readiness including; research and development, medical training and emergency response procedures. AFFRI has been involved in the study of the health effects of embedded uranium in animals as a model for uranium toxicity in level 1 exposed veterans. This has involved the development of analytical methods for the measurement of DU in urine and other biological fluids. Two analytical methods were identified at the meeting between GVIU and AFFRI staff.

a. **ICPMS analysis.** It was indicated that the AFFRI laboratories were analysing DU in urine using a standard Perkin Elmer Elan quadropole instrument. Samples appeared to be pre-concentrated using an ion exchange system before analysis. No details were obtained but the use of ion exchange resins in this way is a standard radiochemical procedure. An example would be the Eichrom UTEVA resin. Unfortunately the planned laboratory visit could not take place due to time constraints so the performance of the method could not be pursued, however level 1 exposure leads to excretion of DU in µg/l quantities. A method developed for the study of such high DU levels is unlikely to be suitable for the ng/l levels expected in the DUOB retrospective study.

b. **Colorimetric method.** AFFRI have also developed a patented colorimetric method for analysis of uranium in urine. The method again uses ion exchange sample concentration followed by a colour reaction with 2-(5-Bromo-2-pyridylazo)-5-diethylaminophenol. The test kit is hand held and is intended as a rapid field test for uranium in environmental samples and biological fluids. The current detection limit is 30µg/l although it is thought this can be lowered to 3µg/l with further development. Again this method, although adequate for its intended purpose cannot be considered appropriate for retrospective analysis.

2.2 **Conclusion.** AFRRI methods are intended for the study of embedded DU and field estimation of excretion immediately post exposure and are comparable to the biological monitoring methods now to be employed by MoD.

3. **AFIP.**

3.1 AFIP is the US tri-service centre of expertise in pathology with a wide ranging remit covering all areas of advanced pathology including toxicology, infectious disease and environmental medicine. Included in this AFIP provides the pathology expertise in the study of Gulf War illness symptoms, including the determination of uranium concentration and isotope ratio in urine samples from DU exposed veterans. AFIP, like AFRRI, has a direct interest in the study of level 1 exposures and has carried out studies on the fate of DU shrapnel in the body.

3.2 **Interlaboratory comparisons.** AFIP has been involved in an interlaboratory comparison trial to assess the performance of the laboratories involved in the analysis of DU in urine samples from Gulf War veterans.

3.3 **DU analysis at AFIP.** Uranium analysis and isotope ratio methods have been developed by a group led by Dr John Ejnik, a lieutenant in the US Navy Medical Corps. The methods for urine analysis involve the use of a Perkin Elmer Elan DRCII ICPMS which is a quadropole instrument with an additional reaction cell before the main mass filter. The use of the reaction cell allows the removal of mass interferences thus giving lower instrument backgrounds and lower detection limits. The instrument is used in its standard configuration using platinum cones and a quartz spray chamber.

3.4 **Total uranium.** Samples are collected in polythene containers that have had minimal pre-cleaning. The samples are then ashed in nitric acid, taken to dryness and re-dissolved in 0.2% nitric acid. U233 is added as an internal standard and the samples are then analysed by isotope dilution mass spectrometry using the Elan ICPMS in normal mode. Results are ratioed to creatinine allowing spot samples to be used.

3.5 **Isotope ratio.** The ^{235}U:^{238}U ratio is measured in urine samples but other isotopes are omitted. Samples are again collected in polythene containers and

are acidified with 5% nitric acid prior to analysis. Analysis is direct using the Elan ICPMS in DRC mode. Several DRC reaction gases have been used including oxygen which forms uranium oxides in the reaction cell and allows measurement of the uranium at masses of 267 and 270. No tracer is used and the analysis can be performed on a 15ml urine sample.

3.6 **Method performance.** Data was presented demonstrating that the method could determine accurate 235/238 isotope ratios in samples containing 3-5ng/l total uranium. No detection limit for total uranium was given but it is assumed that it will be at least an order of magnitude bwer, ie of the order of 0.3ng/l.

3.7. **Conclusion.** The data presented for the DRC ICPMS analysis confirms that this method would potentially be suitable for assessment of current DU excretion by Gulf War veterans.

4. **CHPPM.**

4.1 CHPPM is the US Army's environmental and occupational health organisation. Although based in Baltimore it is active worldwide. Militarily its role is to ensure the health of US soldiers by both preventative measures and by minimising exposure to environmental and toxicological hazards. CHPPM has been involved in the characterisation of DU exposure pathways and the development of awareness training for military personnel to minimise DU exposure in future operational theatres.

4.2 **DU analysis.** CHPPM has investigated a wide range of analytical methods to assess their suitability for determining DU in urine following inhalation exposure and have concluded that ICPMS is the most appropriate. The laboratory currently uses a Perkin Elmer 6000 quadropole ICPMS for determination of total uranium with a detection limit of 1.8ng/l. Samples are prepared for analysis by digestion with nitric acid and hydrogen peroxide and diluted prior to analysis. U233 is used as a tracer and the analysis is carried out by isotope dilution.

4.3 **Sample storage.** Studies are underway to fully evaluate sampling and storage procedures but the use of polythene containers is likely with preservation by acidification or freezing.

4.3 **Isotope ratio.** Current work is based around the use of preconcentration techniques. Samples are separated using the Eichrom UTEVA resin and analysed by ICPMS. Development work is still ongoing.

4.4 **Conclusion.** CHPPM is developing methods for prospective monitoring of personnel in future operational theatres. This is focussed on the ability to identify inhalation exposures and appears to be linked to acceptable radiation exposure limits. As such the methods are comparable with MoD biological monitoring methodology rather than the DUOB retrospective analysis.

5. **VAMC.**

5.1 The Baltimore VA Medical Center is described as the acute medical and surgical care facility for veterans. It combines inpatient, outpatient and primary

care services and also carries out research into medical issues, including depleted uranium exposure studies led by Dr McDiarmid.

5.2 VAMC is involved in two separate studies which are of interest.

a. A cohort study of 39 exposed veterans most of whom are carrying DU shrapnel. Most of these individuals are excreting background levels of uranium.

b. A mail-in study consisting of 450 individuals who provided 24 hour urine samples by post. Data was presented showing that the great majority of samples gave uranium levels of less than 0.05ng/g.creatinine. Judging from the data shown the average uranium excretion was about 10ng/l. This is especially notable as the sample containers used are high density polythene which are issued uncleaned. This strongly suggests contamination was not a problem in this study. Samples for this study are stored frozen and acidified prior to analysis by AFIP.

5.3 **Normal levels.** Dr McDiarmid discussed the availability or normal data for uranium excretion and identified the following ranges and values

a. The US national study carried out by CDC – geometric mean urine concentration, 10ng/l.

b. ICRP urine uranium dietary limit – 365ng/l

c. ICRP maximum background uranium in urine – 15ng/l.

d. DoE occupational decision level for nuclear plant workers – 800ng/l

e. VAMC cut off level, below which isotope ratios are not measured, 100ng/g.creatinine.

6. **Overall conclusions.**

6.1 The following points should be noted.

a. Of the three US methods the AFIP method using DRC ICPMS has the lowest detection limit and can measure isotope ratios at uranium concentrations of a few ng/l. This is directly comparable with the levels expected in the DUOB retrospective study.

b. Creatinine measurements are recommended for all samples to allow spot urine samples to be used.

c. Polythene containers are universal and only minimal pre-cleaning is used.

Dr D Lewis
10 Mar 03

ANNEX D - DU OVERSIGHT BOARD - FINAL TERMS OF REFERENCE

1. The purpose of the Depleted Uranium Oversight Board is to:

a. Oversee and co-ordinate the process of letting the contracts, and undertaking testing, for uranium isotopes in urine to assess historical exposure to DU.

b. Act as a Project Board, to direct, endorse and oversee the work of the MOD Project Manager who will:

(1) Develop a draft Statement of Requirement for a DU sampling protocol, a chain of custody for samples and a quality control protocol for endorsement by the Board.

(2) Invite proposals for testing.

(3) Prepare an assessment of proposals received.

(4) Manage a pilot study to demonstrate the performance, precision, accuracy and validity of the method, including the techniques for collecting, splitting, storing, transporting and analysing samples.

c. If satisfactory methods of testing can be established, agree proposals for one or more epidemiological studies using those methods, to determine the distribution and determinants of excretion of uranium isotopes in urine, and to explore the relation of historical exposure to DU to possible biological and health effects.

d. If satisfactory methods of testing can be established, agree arrangements for testing additional individuals who are not part of the epidemiological studies. These will include the arrangements for the involvement and briefing of GPs, and procedures for any accompanying medical assessment.

e. Monitor progress of the testing, including auditing and quality assurance of the data.

f. Ensure that the findings of the testing and research are appropriately promulgated.

g. Report to the Under-Secretary of State for Defence and Minister for Veterans' Affairs, on progress issues and concerns.

2. The Oversight Board will explore and advise on other possible methods of historical exposure assessment.

3. The Oversight Board will be invited to comment on:

a. The development of biological monitoring tests to be used by MOD for future operations where DU is used.

b. Proposed epidemiological studies to examine possible ill-health effects of service in the Balkans.

c. Possible arrangements for a Veterans' Assessment Centre