NoDARS Project Steering Group
Third Meeting
Stockholm, Sweden
13-14 April 2016

Title	Minutes from the 3rd meeting of the NoDARS Project Steering Group
Submitted by	NDPHS Secretariat (Project Lead Partner, WP 1 Leader) and the Public Health Agency of Sweden (WP 2-7 Leader)
Summary / Note	This document outlines the main discussion points and decisions made during the meeting.
List of Annexes	Annex 1 – List of participants Annex 2 – List of documents submitted to the meeting

1. Welcome and opening of the meeting

The meeting was opened by Mr. Marek Maciejowski, Director of the NDPHS Secretariat (who chaired it during agenda items 1 through 3.1) and Dr. Karin Tegmark Wisell of the Public Health Agency of Sweden, PHAS (who chaired it during agenda items 3.2 through 6). The Host, PHAS, bid the welcome to the participants.

The participants introduced themselves.

2. Adoption of the agenda

The Meeting **adopted** the Provisional agenda (cf. document NoDARS PSG 3/2/1).

3. Implementation of the project Work Packages

3.1 WP 1 – Project management

The WP 1 Leader, the NDPHS Secretariat, thanked all Project Partners for the submission of documents required for the interim report and informed about the progress in submission of documents by the Project Partners thus far, including the progress in submission of financial information (cf. document PSG 3/3.1/1), for the reporting period January – March 2016.

Further, the Secretariat announced that, following their announcement by email, a formal letter was received from the Norwegian Institute of Public Health confirming that this Project Partner had left the project. Following this change, he highlighted that the remaining Project Partners needed to agree on steps to be taken to fulfill the obligations towards the donor. This would include a revision of the description of the action as well as an amendment of the project budget.

Having discussed the different possibilities of redistributing the funds becoming available due to the Norwegian Project Partner's withdrawal from the project, the Meeting **agreed:**

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- Each Project Partner shall carefully consider their organization's needs of additional personnel to ensure the achievement of the project's strategic aim and the project quality. Based on this, the PHAS will propose an amendment of the budget. Should no agreement be reached, the available funding will be distributed proportionally among the Project Partners.
- The budget item "Distribution of questionnaires and material for faecal samples" will be removed and incorporated into another budget item;
- When all inputs regarding the reporting of expenditure on equipment and supplies & other costs, services have been received, the NDPHS Secretariat will approach the donor to discuss the option of transferring the respective budget items into simplified cost options/lump sums.

Further, the Secretariat reminded the Project Partners of the conditions set out in the Grant Contract's General Conditions and Specific Conditions as well as several annexes. In particular, he highlighted the procurement requirements laid down in Annex 4.

With reference to document NoDARS PSG 3/3.1/2, the Secretariat introduced a proposed template for reporting expenditure on equipment and supplies & other costs, services.

Following the feedback received, the Meeting **agreed**:

- The columns "Amount of samples taken" and "Costs per sample (original currency)" would be deleted and replaced with a column "Amount used for NoDARS";
- All Project Partners will send examples of invoices received regarding the respective expenditure as well as inform about their experiences on how such costs were reported by their organizations within other EU co-financed projects to the PHAS by the end of April. Subsequently, the PHAS and the NDPHS Secretariat will work together on improving the reporting template, if applicable.

Key points and changes in study-protocols

- The study period for sample collection and analysis would benefit greatly if extended to the end of 2016 but it needed to be accepted by the beneficiary. To finance the longer period a suggestion will be made to the European Commission to use the funds intended for the Norwegian partner;
- The nitrate test should not be used to exclude diagnosis of lower UTI. If it is causing problems in a given Project Partner's setting it is acceptable to remove it from the inclusion criteria;
- It was decided to allow UTI samples to be collected with the exclusion criteria that the patient should *not* have taken antibiotics for the last 2 weeks (see exception for Poland in section 3.2). The original exclusion criteria (3 months) will still be used by some partners. The change was allowed because of the German 2 week criteria in their ongoing study and because several Project Partners had issues with this exclusion criteria;
- Identification of K. pneumonia from the Chrome ID plates can be complex since many different sorts of species show the correct blue green color. A MALDI-TOF analysis is the most convenient way of checking this but it might not be available for all Project Partners which is why alternative standard methods are also acceptable;.
- Project Partners should keep in mind that it is the number of SAMPLES and not E. coli isolates that is set to 500;

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Further, the Meeting discussed several **budget-related issues** and **took note/decided** as follows:

- RKI has a problem with the employment categories/descriptions, especially the biomedical technician, since they do not have the laboratory within their own organization and the budget chapter do not allow them to use the intended funding for laboratory work for services from another institute with funding coming from within the NoDARS project;
- Some Project Partners (i.e. Russia, Latvia) cannot use the intended funds for samples from outpatient units that are supposed to go to the GPs for collecting the UTI samples. This is due to the organization of the healthcare system by the government in each country;
- Poland and Sweden have issues recruiting volunteers for the fecal study since there is no compensation for the participant (e.g. a small gift like a ticket to the movies). No part of the budget can be used for this. Although it would be beneficial, it is considered a big change in the budget and may be difficult to introduce at this point;
- The Russian Project Partner has problems with documentation of the material used for the UTI and Feces study. Possible solutions to this will be discussed between the PHAS, the NDPHS Secretariat and the IAC of SSMU

3.2 WP 2 – Assessment of true resistance levels in Escherichia coli causing uncomplicated UTIs

First a summary was made by the PHAS of the evaluation sent out beforehand for WP 2 and 3. The summary can be seen in point 3.7 Project evaluation.

Project Partner from Sweden
The PHAS has recruited a university hospital laboratory to do the analysis of the UTI samples. In total 9 primary care centers have been recruited to send in samples. The centers normally send in samples to the university hospital so the flow of samples is the same as the normal one. So far the work flow, collection and analysis work well. The problem is with sample numbers. Most of the centers evaluated that they would provide 10 samples a week which meant that the collection should have been finished in approximately 8 weeks. However, the collection is going very slow and two of the centers have dropped out. At the moment of the PSG meeting around 80 UTI samples (54 E. coli) have been collected. The reason for the slow collection according to primary care is that they have much fewer patients than expected. Season variations and influenza season are given as explanations. The nitrate dipstick test has been excluded due to new sampling routines where the bladder incubation time would be too short for the test to work.

Project Partner from Russia
The IAC of SSMU is in the process of recruiting GPs to provide samples. However, this is turning out to be a difficult process since it is hard to set up contracts that involve transaction of money for samples. There are also problems and uncertainties that it will be impossible to provide the required documentation for the European Commission. All these contract and documentation issues are delaying the start of the collection and at the moment no UTI samples have been collected. The IAC of SSMU also expressed concern regarding the number of samples, i.e. 500, and thought that it was a very ambitious number to collect.

Project Partner from Poland
The IOMEH have recruited a laboratory that does clinical diagnostics of UTIs. The patients come to the clinic voluntarily and leave samples and would then be asked to take part in the study. As

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it turns out most women that come to the clinic has already taken chemotherapeutic agent with antibacterial activity (It is a nitrofurantoin analog furagin (furazidin) classified to nitrofurans) that is available over the counter in Poland. Therefore, it has not been possible to include them in the study due to the exclusion criteria that the patient should not have taken antibiotics for the last three months. The nitrate dipstick test has also caused problems since it is not in the normal routine of the laboratory and they think it takes too much time. At the moment no UTI samples have been collected. A question was raised if we could consider changing the exclusion criteria to also include women that have taken antibiotics specifically in Poland due to the specific circumstances.

The following Poland-specific decisions have been taken (at the meeting and via mail conversation afterwards):

- The IOMEH should try to include as many patients that have **NOT** received antibiotics in the last 2 weeks as possible;
- The IOMEH may include patients that have taken or are on antibiotics if it is impossible to finish the sample collection otherwise.

Four questions should be added to the questionnaire:

1) Have you taken antibiotics at any time during the last two weeks?
2) Are you currently taking antibiotics?

If the response to any of these two questions is affirmative, the patient should also answer the following questions in the questionnaire:

3) What antibiotic substance have you taken?
4) Did you have a prescription from a general practitioner?

Project Partner from Latvia

The PSCUH have recruited 15-20 GPs to collect UTI samples. In November 2015 a pilot study was conducted but no samples were collected. One of the issues is that the communication with the GPs is hard because they promise to deliver things and then they don't follow up. This makes it hard to estimate how many samples will come (if they come at all). The influenza season has also affected the number of UTI patients according to the GPs who are experiencing a high pressure from this patient group. The PSCUH also thinks that they should recruit patients from other units then GPs such as gynaecologists and hospitals since they might have a higher number of UTI patients. So far around 15 UTI samples have been collected.

Project Partner from Germany

The RKI is collaborating with another study that has an ongoing collection of UTI samples from uncomplicated cystitis. The differences are that there is only information about antibiotic consumption during the last two weeks (and not three months) and that there is no questionnaire. It will be possible to extract data based on most of the NoDARS inclusion criteria. Although the RKI approach is different than that of the other Project Partners and some data will be lacking, all Project Partners **agreed** that this is still a valuable dataset to have in the project. Since the original antibiotic consumption exclusion criteria set to three months was not based on any scientific referents but more on discussions during the two workshops it was decided that the limit should be changed to two weeks (as reflected earlier in the current meeting minutes).

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Project Partner from Finland
Jaana Vuopio from the University of Turku (UT) had prepared a presentation about the work which the Finnish partners have done to set up the studies. The UTU works with a health center to recruit UTI patients. Women are asked over the phone to bring in a sample and answer a questionnaire. So far 3 UTI samples have been collected. The problem is that it is hard to motivate the patients to come in and leave a sample since this is an extra effort to the patients. Normally they get a prescription via phone for acute cystitis. The UTU is searching for a new partner to collaborate with. The UTU commented that it would have probably been easier to recruit patients if the exclusion criteria with no antibiotic treatment for three months would not have been there. Also the nitrate test caused problems in their setting.

3.3 WP 3 – Assessment of the penetration of antibiotic resistance in society

First a summary was made by the PHAS of the evaluation sent out beforehand for WP 2 and 3. The summary can be seen in point 3.7 Project evaluation.

Project Partner from Sweden
The PHAS is working with two elective surgery units that will recruit patients for the study by handing out kits. So far 8 samples have been collected. The setup is failing at both places because of different reasons. The main reason is that the patients do not seem to be interested in participating. The response rate is very low. At one of the places the flow of information is not workings since it is too close between when they get the kit and when they will go in for surgery. For the student group the sampling is starting in May 2016 and 2-3 lectures are planned. There is a worry that since there is nothing in it for the volunteers to participate, it will be hard to collect the needed number of samples even if the collection period is prolonged.

Project Partner from Russia
The IAC of SSMU is the first Project Partner to have finished a sample collection. 250 fecal samples from students, out-patients and healthy volunteers have been collected and analyzed. The accompanying questionnaires have also been filled out. The main problem for the IAC of SSMU is documentation of how the funds have been spent.

Project Partner from Poland
The IOMEH have not collected any fecal samples at this moment. The activity of the IOMEH has been focusing on organizing the cooperation with the primary care units as well as needed reagents and media supply. The late in collecting samples was caused, among other things, by unexpected breaks in the project leader/the microbiologist work.

Project Partner from Latvia
The PSCUH are working together with a surgical unit to recruit patients. It has been challenging to find patients that are not on prophylactic before the surgery. So far 12 samples have been collected from this unit. Since the setup is not really working the PSCUH is attempts to recruit units with different kind of surgeries like nose, eye and/or orthopaedic clinics. Although the collection has been slow PSCUH is still optimistic that something will come out of this part.

Project Partner from Germany
The RKI is also combining this part with another study that is looking at travel-associated carriage. They recruit study subjects from a vaccination clinic and screen all participants before travel. These results could be used as a measure of the prevalence in society. Since many young people travel the age span should also cover the student group.

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Project Partner from Finland
The UTU is recruiting outpatients through orthopedic and surgery units. A research nurse has also been recruited to approach potential volunteers. Also, students have been recruited via university lectures. In total, after 2-month recruitment at the orthopedic clinic and 10 recruitment visits to lectures, 50 fecal samples have been collected. At the moment new routes have been activated to continue the collection. The UT feels optimistic that this collection is possible to finish even though there has been a lot of work to get it going.

3.4 WP 4 – Assessment of guidelines for the treatment of uncomplicated urinary tract infections

Two tools were presented for this work package. Mr. Oliver Dyar, who has worked on the tools, was present and talked briefly about their background.

The first tool is intended to be used for evaluating treatment guidelines based on all Project Partners results in the project (antibiotic selection tool). It was after discussions agreed by all Project Partners that the tool should also contain information about the susceptibility in complicated UTIs. If that data were not available, resistant rates for bloodstream infections should be entered. All Project Partners also discussed and decided that availability and price should be more extensively added. All Project Partners decided that the PHAS should make a revised version and send it out to all Project Partners in mid-May 2016.

The second tool was a modified Agree II scheme that had been designed to evaluate the quality of existing guidelines i.e. the evidence and process behind the guidelines. This tool is completely unrelated to the appropriateness of the selected antibiotic and is a standalone tool towards the other work packages. Project Partners generally commented during the meeting that it was difficult to relate this part to the rest of the project since it has another aim compared to the rest of the project. It was also hard to see who, in each country participating in the project, should fill it out since at least three people are needed to get a comparative analysis. Some Project Partners also thought that it might be hard since the persons approached to fill in the agree tool might look at it as critique towards the guidelines. Also, only three participating countries (Finland, Germany and Sweden) have the type of guidelines that could be evaluated according to this scheme. Because of this discussion and subsequent internal discussions at the PHAS, the latter decided that the tool should be put aside for the time being.

3.5 WP 5 – Assessment of AMR-strategies

For this work package one tool had been created. The initial reaction from Project Partners was that it was a bit too long and extensive and that it should be revised according to what is relevant in the project. However, it should still be a comprehensive standalone tool. Most Project Partners thought that the WHO agenda, which stipulates that each country should have national action plans before May 2017, would not make a major difference on the outcome of the answers in the questionnaire. A revised suggestion will be made by the PHAS and sent out in mid-May 2016.

3.6 WP 6 – Dissemination of project results

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A discussion about how results produced in each country could be used by each Project Partner individually and what sort of publications the Project Partners would expect to get out of the project, resulted in the following conclusions:

- The result may be used in each country for submission of abstracts and publication in a way that does not form a conflict with the NoDARS interests of future publications results in scientific journals. The exact same dataset that is planned for NoDARS compilations cannot be used in other publications. Parts of the dataset can be used but need careful consideration and need approval of the NoDARS PSG.
- For Germany, which is combining NoDARS with other studies, the aim will be similar but the NoDARS Project will only use a subset of the collected samples. The other German study will most likely be published first but if not, the NoDARS publication should not be delayed due to proprietary issues regarding data.
- Drafts of what the NoDARS Project Partners expect to include in each publication should be started at the PHAS as well as a suggestion on how many writers it is reasonable to include from each country.

3.7 WP 7 – Project evaluation

Summary of evaluation
The PHAS, in its capacity as the Lead Partner for WP 2-7 summarized the output from the evaluation made on the progress made by Project Partners. The following questions were included in the evaluation:

1. What is your current status of sample collections? I) UTI and II) feces
2. What problems/difficulties do you face in connection to collecting samples/questionnaires?
3. If you have difficulties can you see/suggest any solutions?
4. At the moment, do you feel that the timeline to finish the collection before October is realistic?

Project Partners experience different problems due to differences in healthcare systems in their countries but most problems can be summarized as belonging to the following categories:

- Slow collection because of fewer samples than approximated;
- Study population defined hard to reach/work with;
- Study subjects not interested in participating;
- Flow of samples is not working;
- Documentation is to demanding/complex;
- Most study subject have taken antibiotics;
- GPs not interested in taking part in study;
- Dropouts of collection centers/persons

None of the Project Partners thought that they would have finished the sample collection by October this year except for Germany.

4. Any other business

No other business was discussed.

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5. Adoption of the NoDARS PSG 3 meeting minutes

The meeting **agreed** that the NDPHS Secretariat would send out draft PSG 3 meeting minutes to the participants no later than 9 May 2016 and that comments on the draft would be due, at the latest, on 16 May 2016. The revised minutes would be distributed on 18 May 2016 to be adopted *per capsulam* provided that no further comments are submitted until 25 May 2016.

6. Closing of the meeting

The Meeting was terminated on 14 April 2016 at 12:00 hours.

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