***PIVOTAL ASSESSMENT OF THE EFFECTS OF BIOACTIVES ON HEALTH AND WELLBEING. FROM HUMAN GENOMA TO FOOD INDUSTRY***

Grant Agreement Number 311876

**PATHWAY-27 Second Annual Meeting**

**Bologna (Italy), 10-12 March 2015**

Alma Mater Studiorum - University of Bologna

Palazzo Hercolani, Strada Maggiore 45

# Minutes

## Summary

# AGENDA

## Day 1. Tuesday March 10

**Section I - Participants: Consortium members + SAB and IP members**

1.30 – 2.00 pm: **Welcome and overall presentation of the project -** Alessandra Bordoni

2.00 -2.30 pm: **WP2. State of the art -** Didier Dupont

2.30 – 3.00 pm: **WP4. State of the art -** Juhani Sibakov

3.00 – 3.30 pm: **Discussion**

3.30 – 4.00 pm: **Coffee break**

4.00 – 4.30 pm: **WP3. State of the art -** Lidia Tomas

4.30 – 5.00 pm: **WP5. State of the art -** Luigi Ricciardiello

5.00 – 5.30 pm: **WP6. Brief overview of activities foreseen in WP6 -** Didier Dupont and Francesco Capozzi

5.30 -6.00 pm: **Discussion**

6.00 pm: **Social activities and dinner**

## Day 2 – Wednesday March 11

**Section II - Participants: Consortium members + SAB and IP members**

9.00 – 9.30 am: **WP7. State of the art -** Stephane Vidry

9.30 -10.00 am: **WP8. State of the art -** Andras Sebok

10.00-10.30 am: **The "train the trainers" trainings in PATHWAY-27 -** Andras Sebok

10.30-11.00 am: **Discussion**

11.00 -11.30 am: **Coffee break**

**Section III - Participants: Consortium members only**

11.30 am -1.00 pm: **WP4/WP2 incoming activities + discussion -** Juhani Sibakov and Didier Dupont

1.00 – 2.00 pm: **Lunch**

2.00 -3.00 pm: **WP7 incoming activities + discussion -** Stephane Vidry

3.00 – 4.00 pm: **WP8 incoming activities + discussion -** Andras Sebok

4.00 – 4.30 pm: **Coffee break**

4.30 – 5.00 pm: **WP5 incoming activities (and connections to WP6) -** Luigi Ricciardiello

5.00 – 5.30 pm: **WP6. Incoming activities -** Clarissa Gerhauser

5.30 – 6.30 pm: **Discussion on WP5 and WP6 activities**

6.30 pm: **Social activities and dinner**

## Day 3 – Thursday March 12

**Section IV - Participants: Consortium members only**

9.00 – 9.30 am: **WP3. Incoming activities and connections to WP6 -** Lidia Tomas

9.30 – 10.30 am: **Discussion on WP3 activities and connection between *in vitro* and *in vivo* studies**

10.30 -11.00 am: **Coffee break**

11.00 – 12.00 am: **WP1. Incoming activities and discussion -** Alessandro Zamboni, Alessandra Bordoni

12.00 am – 1.00 pm: **Summary of the meeting, all other business and concluding remarks -** Alessandra Bordoni and Coordination Support Team

1.00 pm: **End of the meeting**

# PARTICIPANTS

| Partner N. | Partner | Name | Surname | 10 March 2015 | 11 March 2015 | 12 March 2015 |
|---|---|---|---|---|---|---|
| 1. | UNIBO | Alessandra | Bordoni | x | x | x |
| 1. | UNIBO | Luigi | Ricciardiello | x | x | x |
| 1. | UNIBO | Andrea | Gianotti | x | x | x |
| 1. | UNIBO | Francesco | Capozzi | x | x | |
| 1. | UNIBO | Alessandro | Zamboni | x | x | x |
| 1. | UNIBO | Silvia | Garelli | x | x | x |
| 1. | UNIBO | Francesca | Danesi | x | x | x |
| 1. | UNIBO | Veronica | Valli | x | x | x |
| 1. | UNIBO | Claudia | Pacciolla | x | x | x |
| 2. | INRA | Didier | Dupont | x | x | x |
| 2. | INRA | Jean-Louis | Sebedio | x | x | x |
| 2. | INRA | Corinne | Malpuech-Brugère | x | x | x |
| 2. | INRA | Carlos | Pineda Vadillo | x | x | x |
| 4. | MRI | Achim | Bub | x | x | |
| 4. | MRI | Alice | Arianna | x | x | x |
| 5. | VTT | Juhani | Sibakov | x | x | x |
| 6. | DKFZ | Clarissa | Gerhauser | | afternoon | x |
| 7. | ULE | Caroline | Orfila | x | x | x |
| 9. | AINIA | Lidia | Tomás | x | x | x |
| 10. | CRNH | Noël | Cano | x | x | x |
| 10. | CRNH | Adeline | Blot | x | x | x |
| 12. | EGE | Sedef Nehir | El | x | x | |
| 12. | EGE | Sibel | Karakaya | x | x | |

| | | | | | | |
|---|---|---|---|---|---|---|
| 13. | CBHU | Andras | Sebok | x | x | |
| 13. | CBHU | Adrienn | Hegyi | x | x | x |
| 13. | CBHU | Kertész | Zsofia | x | x | x |
| 14. | ILSI | Stéphane | Vidry | x | x | x |
| 14. | ILSI | Peter | Putz | x | x | x |
| 15. | LVA | Christine | Grabler | | x | |
| 16. | JRC-IHCP | Stefan | Storcksdieck | x | x | x |
| 17. | IFN | Nick | Henson | x | x | x |
| 18. | AdWare Research | Monika | Muller | x | x | x |
| 18. | AdWare Research | Bence | Bàlint | x | x | x |
| 18. | AdWare Research | István | Richter | x | x | x |
| 19. | GIOTTO | L. | Tenori | x | x | x |
| 20. | NGB | Alberto | Santini | x | x | x |
| 21. | ASL | Gerard | Pieroni | x | x | x |
| 21. | ASL | Mohamed | Gad | x | x | x |
| 22. | ABRO | Marisa | Sanz Buenhombre | | x | x |
| 23. | SOF | Frédéric | Prothon | | x | x |
| 24. | ADEXGO | Tamas | Toth | x | x | |
| 24. | ADEXGO | Hajnalka | Hingyi | x | x | |
| ***SAB*** | ***EFSA*** | ***Silvia*** | ***Valtuena*** | ***x*** | | |

## Minutes

*Please note that all the presentations showed during the meeting are uploaded into the restricted area of project website in the following section: General Info > Pathway-27 Project Meetings> 2nd Annual Meeting*

## Section I

**Welcome and overall presentation of the project (Alessandra Bordoni -UNIBO)**

Alessandra describes the general structure of the project (objectives, workplan, expected results, etc.) and introduces three new members of the UNIBO team and one of INRA-Clermont / CRNH team.

Then Alessandra begins to explain the current activities of the project and stresses in particular that the pilot studies give not only the possibility to reduce expenses related to larger intervention study, but are mainly a tool to find and solve all the problems concerning the procedures (e.g. BEF delivery to recruitment centres, storage, compliance, volunteers' biological samples, etc.) that will be used in the Large Intervention Study (LIS). In fact, the same procedures will be used in the LIS, and their implementation during the pilots will help to run the LIS without delays. Since PATHWAY-27 is not entitled to ask an extension of the duration, it is very important that the LIS will not go beyond the scheduled plan.

| Issue | Related WP | Decision taken |
|---|---|---|
| **Delay in the Milkshake Pilot** | WP5 | Reduced time will be available for the LIS recruitment. Recruitment centres will try to speed up the procedures and will inform WP5 leader and Coordinator in case of problems |
| **Industrial platform enlargement** | WP1 | The addition of new members to the IP must be voted on by the General Assembly from now on. Standard procedure as set in the Consortium Agreement applies. |
| **Next annual meeting** | WP1 | The meeting will be held in Budapest (approx. March 2016). CBHU will take care of the logistics |

Alessandra reminds the Consortium that publication and dissemination rules have been already agreed and are available from the project website (see presentation); they must be carefully followed before the submission of both abstracts to meetings and manuscripts for publication in scientific journals. Furthermore, after the meeting the poster/presentation must be sent to CBHU to allow its uploading on the website, and manuscript acceptance for publication must be communicated to the Coordinator and CBHU.

Alessandra also notes that the PATHWAY-27young researchers mobility scheme is a great opportunity, and invites all consortium partners to carefully consider to send their young

researchers to other Institution, and to be available to host foreign researchers. UNIBO will be happy to do so.

**WP2 State of the art (Didier Dupont -INRA)**

Didier shows the structure of the work package (objectives, tasks, participants, workplan, etc) and provides a description of the procedure from the 45 initial foods to the 15 foods used for the pilots.

The main problems encountered during BEF selection were related to stability/shelf life, bioactive content after processing, and nutritional profile of the food. A prescreening of sensory quality and consumer acceptance was performed before the planned scheduling to exclude BEF with no chance to be selected; consequently the development of breadsticks, egg beverages and puddings were stopped, thus saving money and effort. Didier presented a summary of the different characteristics of the developed BEF

All deliverables foreseen in WP2 have been submitted except for D2.5. It will be submitted as soon as results of the challenge test of bakery products are available.

All the WP2 tasks are almost finished except for T2.4 which need to be prolonged due to the need of verify the bioactive content and retention in all BEF batches produced for the pilot study.

| Issue | Related WP | Decision taken |
|---|---|---|
| **T2.4 extended duration** | WP2 | The General Assembly agrees that the WP2-T2.4 will end in M54. The Coordinator will ask the Officer for the extension of T2.4 |

**WP4 State of the art (Juhani Sibakov -VTT)**

Juhani shows the structure of the work package (objectives, tasks, participants, workplan, role of companies, etc.). Milestones and deliverables were achieved on time and the production/delivery schedules of the three types of BEF are ready.

The limited production of biscuits (75 instead of 120 packages) will lead to the need of a third batch depending on the recruitment rate of volunteers, therefore the recruitment centre have to promptly inform the WP leader if more biscuits are needed.

The pilot production of BEF seems to be affected by some issues that have to be managed in order to limit the impact on the clinical studies.

Although the clinical results of the pilot studies will be the main factors in the selection of BEF to be used in the LIS, also the industrial production problems will be taken into consideration. Silvia Valtuena (EFSA – SAB member) expresses some concern regarding the placebo food since they have significantly different appearance from the BEF.

The consortium explains that the issue was already internally discussed and that the procedure that will be adopted will overcome this problem.

In particular, a clear separation will be ensured between the front personnel in contact with the BEFs study participants and the investigators in charge of data collection and analysis, in order to keep blind the whole experimental plan.

| Issue | Related WP | Decision taken |
|---|---|---|
| **BEF production issues** | WP4 | Issues will be managed in order to have a limited impact on the clinical studies |

**WP3 State of the art (Lidia Tomas -AINIA)**

Lidia shows the structure of the work package (objectives, tasks, participants, workplan, etc.). Task 3.1, 3.2 and 3.3 have been concluded.

In particular, the database is available and running.

Regarding the effects of bioactives on cultured adipocytes and hepatocytes, experimental conditions and results are reported in details in the presentation.

**WP5 State of the art (Silvia Garelli - UNIBO)**

Silvia shows the structure of the work package (objectives, tasks, participants, workplan, etc.) with a particular focus on the new inclusion criteria, on the database, and on the pilots-related procedure (see presentation).

Noel Cano (CRNH) informs that in his recruitment centre the inclusion of volunteers in pilot studies only began on February 2015 instead September 2014 due to the lateness of the preclinical phases of the project, and. At present the number of recruited volunteers is lower than foreseen.

To avoid the same kind of problem during the LIS, it is strongly suggested to start the screening of possible volunteers immediately and prepare the application for the local ethical committee considering the whole list of BEFs. Upon selection of the most effective enrichment within each pilot, and before the submission of the protocol to the local Ethical Committee, only the selected BEFs will be included in the request for ethical approval.

Noel informs that in France a list of volunteers to be screened can be prepared. However, the screening itself cannot be initiated before getting ethics authorization.

| Issue | Related WP | Decision taken |
|---|---|---|
| **Delay/amendment of the ethical committee approval** | WP5 | prepare the application for the local ethical committee with a list of all the possible BEFs to be used (not only the ones chosen at the end of the pilots) |
| **Delay in the recruitment** | WP5 | start the screening of possible volunteers immediately |

**Brief overview of activities foreseen in WP6 (Francesco Capozzi – UNIBO on behalf of Clarissa Gerhauser - DKFZ)**

Francesco reminds the main aims of WP6 and its interlinking with WP3. This was made even stronger after the modifications of the planned activities based on the suggestions made by the

Project Reviewers (see the consortium's official answer to the Consolidated Review Report). Even if WP6 has not yet started, a detailed planning of its impact on the LIS (and Pilots) has to be agreed upon.

The additional work, consisting in measuring the concentration of the bioactive compounds, or their metabolites, in plasma could be done using different techniques (e.g. NMR, HPLC, etc) which differ in cost, sensitivity, preparation time and number of detectable metabolites and approach (Quantitative vs. Chemometric Pattern). In particular, NMR spectroscopy is available within the consortium and the partner GIOTTO is willing to perform, in kind, the extra-analyses requested by the Reviewers. Nevertheless, it is possible that NMR could not detect the compound of interest, thus other techniques (e.g. GC or HPLC, even coupled to MS) must be considered as alternative solutions.

Alessandra confirms that UNIBO is available to run the gas-chromatographic (GC) analyses for the quantification of DHA in blood, but there is the need to share this activity (in kind additional activity) with other partners since the number of analyses is too high even considering subgroups of volunteers in each pilot.

Jean Louis Sebedio (INRA-Clermont) confirms that INRA-Clermont could do the GC determination of DHA plasma concentration on samples derived from French volunteers.

Stefan Storcksdieck (JRC-ISPRA) offered to explore the availability of laboratories within the JRC for the quantification of DHA and metabolites of anthocyanins and beta-glucan.

| Issue | Related WP | Decision taken |
|---|---|---|
| **Additional analyses repartition within the consortium** | | UNIBO and INRA will perform GC analyses to detect DHA concentration in volunteers plasma or serum. JRC will check if they can do part of the GC analyses, as well as the HPLC-MS analyses to detect anthocyanins and beta-glucan metabolites. |

**Brief overview of activities foreseen in WP6 (Didier Dupont - INRA)**

Description of the procedure with pig (see slide).

## Section II

**WP7 State of the art (Stephane Vidry – ILSI, and Andras Sebok – CBHU)**

Stephane shows the structure of the work package (objectives, participants, etc.) and clarifies that the last two tasks are more related to the latter part of the project. The guidance paper workshops are going to be organized by JRC in Brussels towards the end of the project (Month 54 or 57), most probably back-to-back. Previous experience of ILSI make possible the settlement of a strong knowledge and a good network of experts and this is the background of the new guidelines. ILSI performed an analysis of the DoW to identify the "feed" for the guidance. Peter will take care of this (and network consultation). New initiative at ILSI could also help (see slide for details).

Andras explains that the guidelines shall be targeted to the type of audience, e.g. no details about science have to be present in the guide for industry (only a layman's report) but there will still be cross-reference between the two guidelines.. A good idea could be a sort of differential profile for each possible end-user together with an electronic version of the guideline. In this way each end

user can choose his/her own profile and print or read only the chapter or page she/he really need. Previous experiences show that the guide likely needs 3-5 rounds of discussion before the final version and Andras suggests that the latter 2 are open to public consultation. See slide for the most common problems encountered in such activities and for the PATWAY-27 specific cases.

**WP8. State of the art - (Andras Sebok – CBHU)**

Andras shows the structure of the work package (objectives, tasks, participants, workplan, etc.), see slide for all details. Andras explains that it is strategic to have a list of project messages or contents that can be promptly disseminated to industry and policy makers because the occasions happen very quickly and there is no time to prepare this kind of content on the spot. Andras underlines that the webinar before the meeting with a discussion of the guideline content is the basis of the training material.

**"Train the trainers" course - (Andras Sebok – CBHU)**

Andras explains the concept of the trainings in the 2 phases of the course and the general objectives. Main aspects and details are reported in the presentation (see slide). Andras underlines that products that seem problematic from the very beginning of their development are not attractive for business. Moreover he suggests repeating the shelf life studies every time the recipe, the packaging or the production technology is modified and in each case at least with two independent production samples.

## General Assembly voting procedure

1. Does your institution approve a budget shift of 4.500 € (EU contribution) from DLP to AINIA regarding activities initially foreseen by DPL as subcontract that, according to FP7 rules, can and have to be performed within the consortium?
2. Does your institution approve a budget shift of 6.440 € (EU contribution) from CRNH to INRA to fix a clerical mistake in the financial form relative to the second amendment.

| Voting beneficiaries: 20 | Quorum: 17 | The decisions are valid |
|---|---|---|
| | YES | NO |
| **first voting** | 20 | 0 |
| **second voting** | 20 | 0 |

The General Assembly approves both the budget shift. The Consortium Plan are Consortium Budget are modified accordingly.

## Section III

**WP4/WP2 incoming activities + discussion**

Didier informs that the publication strategy relative to the WP2 results will be discussed in the next weeks but most probably one manuscript per food category will be written.

The General Assembly agrees on the necessity to prolong the duration of WP2 and in particular of its task 2.4 until month 54. The Consortium Plan will be modified accordingly

In order to have the BEFs available without problems/delays during the LIS it is clear that the dimension of the batch have to be carefully decided taking into account safety, risk and technical limits, storage capacity. For the producers a single batch is preferable but due to shelf-life and logistics limits seem inevitable to have two or more batches. Moreover, even if frozen food and powders are not supposed to have shelf life problems, longer storage studies are needed, to verify the possibility to store BEF for longer time, thus reducing the number of production batches needed for the LIS, the determination of bioactive concentrations in BEF after longer storage time is in progress.

In the first production batch bioactive concentration in BEF will be analysed at 7, 28, 35, 42, 40 and 56 days after production. In further batches, bioactive concentration will be analysed at T7 and at the longer storage time evidencing a good bioactive retention. In case T56 will still evidence good bioactive retention, analysis will be extended till T70 or even longer storage time. As well, microbiological safety and sensory characteristics of BEF will be analysed.

Juhani, as WP4 leader, will take care to set the details in separate discussions and to inform the rest of the consortium of the decision taken and/or problem and possible solutions. Storage capacity of recruiting centers shall be taken into consideration, as well as the storage capacity at volunteers' home.

| Issue | Related WP | Decision taken |
|---|---|---|
| **Food production** | WP4 | Food production constrains and necessities of BEF administering to volunteers shall be made compatible. Details of production scheduling will be set in future separate discussion |
| **Food stability** | WP4 | Prolonged shelf life studies are needed |
| **T2.4 extended duration** | WP2 | The General Assembly agrees that the WP2-T2.4 will end in M54. The Coordinator will ask the Officer for the extension of T2.4 |

**PATHWAY-27 products and the actual EC regulations (Mohamed Gad – ASL)**

Mohamed explains his point of view on the opportunity to launch new food products based on PATHWAY-27 results. He underlines the need to find a shared strategy very soon to benefit from the favourable conditions present within the project, and to be ready to commercialize products at the end of the project. See presentation for details.

Alessandro Zamboni (UNIBO) reminds that the rules governing this kind of exploitation of project results are defined in the Consortium Agreement and in particular in art. 8 (Foreground), therefore suggests to all the Consortium members (it is Alessandra's opinion that all consortium members make an intellectual contribution in generating this Foreground) to alert their respective legal offices to be ready to discuss a Joint Ownership Agreement. Adrienne Hegyi (CBHU) adds that probably at the end of the project new health claims could be approved by EFSA on BEF developed within the project.

| Issue | Related WP | Decision taken |
|---|---|---|
| **Commercialization of PATHWAY-27' BEFs** | WP8 | Joint Ownership Agreement and an exploitation strategy shall be proposed and discussed well before the end of the project |

**WP7 incoming activities + discussion (Peter Putz – ILSI)**

Peter explains the general context underpinning the need to have clear guidelines on health claims. Type of claims and related EFSA statistics are shown (see presentation). The structure of the PATHWAY-27 guidelines is shown together with a first approximation of the consortium members that can contribute to specific chapters. Data collection will be both internal to the project and external thanks to the networks and initiatives where ILSI is actively involved (see presentation for details).

The need to have guideline friendly for industrial users, i.e. very different from guidelines dedicated to scientific community, is underlined.

| Issue | Related WP | Decision Taken |
|---|---|---|
| **Assignment of Guideline sections** | WP7 | Each partner have to confirm their involvement in the respective section, but every partner could be asked to collaborate or provide inputs (each partner has effort in WP7) |

**WP8 incoming activities + discussion (Andras Sebok – CBHU)**

Andras shows the incoming activities and foreseen problems till M38. New procedures for the update of dissemination plan, deadlines for providing available results, website update methods are presented together with all the detailed activities foreseen in WP8 tasks (see presentation for details). Partners are encouraged to take part in the mobility scheme.

| Issue | Related WP | Decision taken |
|---|---|---|
| **Dissemination events** | WP8 | CBHU and JRC will take care of dissemination activities. In order to make partners aware of relevant events to present PATHWAY-27 results and activities, the upload of the event on the project website will be made easier. Furthermore, Stefan will send monthly e-mail alerts to all partners listing the main events of interest, together with information and deadline for abstract |

| | |
|---|---|
| | presentation. Partners interested in presenting PATHWAY-27 related results at an event should inform the coordinator and CBHU. Abstract writing and submission will follow the Consortium rules. All partners are invited to send Stefan information on upcoming events, and to actively participate in dissemination. |

**WP5 incoming activities (Luigi Ricciardiello – UNIBO)**

Luigi focuses his presentation on the Large Intervention Studies (LIS). The prerequisite is the conclusion of the pilot studies but in the meantime many activities such as the definition of the LIS protocol, standard operating procedures (SOPs) for collection and storage of samples, preparation of documents for ethical committee, etc, can be implemented in order to be "ready to start" immediately after the end of the pilots. See presentation for deadline and priorities.

Some SOPs, shown in red in the presentation (see slide), have to be confirmed/agreed upon. Furthermore, there are questions related to the need of performing cross-laboratory validation of blood tests. It is also important to involve WP6 participant to define SOPs for sample collection/storage/shipment, etc. and to have a complete database.

Particular attention shall be put on the food delivery to recruiting centers taking in consideration also the scheduled delivery to volunteers and the storage capacity (both of the center and of the volunteers' home)

Caroline Orfila (ULE) says that they likely won't reach 100 volunteers in their pilot, but they would like to continue the study, since it is possible to find some relevant results. The main difficulty is in the preparation and storage of frozen pancakes that are keeping people from enrollment. She also points out that adding total cholesterol in the inclusion criteria would significantly increase the number of volunteers. Noel Cano reports that in CRNH recruitment is more difficult than foreseen. Achim Bub (MRI) suggests rethinking the inclusion criteria for the LIS. Luigi remains open minded on this but firstly there is the need to find possible solutions (e.g. type of volunteers that partners feel can be recruited; type and number of endpoints (adding total cholesterol) since inclusion criteria were already modified.

Luigi underlines that in another project it was discussed that the threshold for non compliance is set at 60% at it is in many pharmacological studies

| Issue | Related WP | Decision taken |
|---|---|---|
| **Cross-laboratory validation of blood tests** | WP5 | MRI has blood samples from a different study that can be used for the cross validation |
| **DEXA** | WP5 | Already planned at UNIBO and MRI for the LIS. Also CRNH agree to perform it. |
| **Compliance** | WP5 | The threshold for non compliance is set at 60% as it is in many pharma studies |

**WP6. Incoming activities (Clarissa Gerhauser – DKFZ)**

Clarissa describes the tasks planned within WP6 and the interaction with WP3 and WP5 (see slide for details). Alessandra informs the Consortium that UNIBO and NGB are already performing a literature review in order to select the single nucleotide polymorphisms (SNPs) that will be evaluated in volunteers during the LIS. According to the DoW, SNPs related to the risk of the onset of the metabolic syndrome will be selected; in addition UNIBO and NGB suggest to consider SNPs on genes involved in absorption/metabolism of DHA, AC, and BG. Clarissa agrees that it makes sense to have both, and Lidia underlines that in the DoW it is only talked about metabolic syndrome so option 2 would be an extra.

## Section IV

**WP3. Incoming activities and connections to WP6 (Lidia Tomas - AINIA)**

Lidia shows ongoing task and incoming deliverables. She goes into details for experimental setup and conditions (see slide for details) and explains the results obtained so far. Alessandra reminds that in order to increase the connection between WP3 and 6, NMR analysis will be performed by GIOTTO on cultured hepatocytes supplemented with DHA, protocatechuic acid (the main AC metabolite) and propionic acid (the main BG metabolite). Supplemented cells will be provided by UNIBO. This activity is an additional, in kind activity that has been agreed after the mid term review; at present preliminary experiments are already running to set up the best analytical conditions.

A separate presentation (see slide) contains the suggested protocol to measure adipocyte-specific markers proposed by Karolinska Institute in subtask 3.2.1. All partners agree on the protocol, and on the prolongation of the subtask. The Coordinator will ask the Officer to postpone the related D3.4. As well, on behalf of WP3 participants she will ask to skip activities related to the evaluation of apoptosis in adipocytes, since they were foreseen in subtask 3.2.1 to evaluate possible bioactive cytotoxicity. Cytotoxicity has been already determined, and non-toxic bioactive concentrations have been used in further experiments. Therefore experiments on apoptosis are useless, and it will be asked to change them to experiments related to the choice of a suitable model of cultured adipocytes for epigenetics analysis. In fact, the amount of DNA that can be obtained from primary adipocytes is too low for epigenetics, hence there is the need to use a cell line. The consortium agrees on these modifications of WP3 plan.

The length of the exposure of cultured cells to bioactives is discussed. At present, cells are supplemented with bioactives for 6, 24 or 48 h, but Clarissa explains that a longer exposure time is needed for epigenetics experiments. Alessandra agrees; different exposure times will be used by UNIBO on hepatocytes to allow DKFZ the selection of the best conditions.

| Issue | Related WP | Decision Taken |
|---|---|---|
| **Activities of KI in subtask 3.2.1** | WP3 | The Consortium agrees on the activity plan proposed by KI, and to postpone the related D (pending Project Officer agreement) |
| **Time-length of cell supplementation for epigenetics experiments** | WP3 | Different exposure times will be used by UNIBO on hepatocytes to allow DKZF the selection of the best conditions |

**WP1. Incoming activities and discussion (Alessandro Zamboni – UNIBO)**

Alessandro explains that a new procedure for the signature of financial forms (e-signature) will be implemented for the next report. Except this, the reporting procedure is the same as last summer and also the timing is the same (end of the reporting period on the 30th of July, reports ready by the end of September).

Since there is the necessity of an amendment to the Grant Agreement to obtain the e-signature, all the partners are warmly invited to check their incoming activities, and see if modification of the Consortium Plan/Budget is needed with a particular attention to unforeseen subcontracting.

The consortium is informed of the change in the VTT's internal organization (UTRO).

Details on payment procedure and rules for a correct financial reporting are included in the presentation for future consultation (see presentation).

| Issue | Related WP | Decision taken |
|---|---|---|
| **Necessity of an amendment to the Grant Agremment to obtain the e-signature** | WP1 | Partners will check the DoW. If needed, modifications in their incoming activities, D and milestones deadlines, Consortium Plan/Budget (with a particular attention to the unforeseen subcontracting) will be introduced in the amendment |