Final Report Summary - MOTIF (Microbicide Optimization Through Innovative Formulation for Vaginal and Rectal Delivery)

Executive Summary:
The MOTIF project has developed approaches to formulation of anti-retroviral drug (ARV) based microbicides against HIV-1 that optimise the tissue distribution of the drugs and solve the problem of combining physicochemically incompatible drugs in a single formulation. The project also investigated the role of drug transporters in the distribution of ARVs in mucosal tissue and the potential to modify formulations so as to optimise such.

Two formulations based on dissolving films and coating of microcrystalline cellulose beads (Cellets®) were produced that allowed darunavir and tenofovir to be segregated within a single vehicle. The Cellets®-based formulations showed improved stability (particularly at the higher temperature of 40ºC) compared with the dissolving films while in vitro dissolution profiles of the drugs were similar in both formulations. Drug release from the formulations has also been tested in animal models. In rabbit vaginal and anal tolerance studies, both formulations were well tolerated with signs of only minimal irritation partially related to administration.

In parallel studies, expression of drug transporters that may influence the tissue distribution of the ARVs was shown to be largely similar in humans, non-human primates (model used to measure efficacy of drugs) and rabbits (model used to assess tolerance to drugs). Permeability studies using cellular models of human barrier epithelium indicated that tenofovir and dapivirine diffuse passively across the epithelium. Diffusion of Tenofovir was by the paracellular route and of dapivirine was by transcellular routes. In contrast, in colorectal epithelium, darunavir permeability may be limited by the P-glycoprotein and MRP-2 efflux transporters. Uptake of darunavir (apical to basolateral transfer) was increased by addition of inhibitors of the efflux transporters. No unfavourable drug-drug interactions were evident.

The effect of exposure to ARVs, inflammatory cytokines or commensal microorganisms on expression of drug transporters was investigated in human epithelial cell lines. Expression of P-glycoprotein was significantly up-regulated by exposure to inflammatory cytokines but was not affected by other conditions. MRP2 expression was not significantly altered by any of the stimuli. Relatively complex alterations in expressions of other transporters were evident with potential to modulate uptake of some ARVs.

Antiviral activity of the drugs both singly and in combination was determined in ex vivo cervicovaginal and colorectal human and macaque tissues. These studies clearly show that drug combinations show higher efficacy compared with single drugs. The tissue explant models were also used to assess tissue compatibility of the drugs using multiplex assays to measure the effects of exposure to drugs on a panel of 32 immunological markers that included cytokine, chemokines, growth factors and antimicrobial proteins. In cervicovaginal tissue, none of the markers were altered by drug exposure. In colorectal tissue, some changes in levels of 3 markers were observed.

Overall, this project has developed a procedure for stable co-formulation of physicochemically-incompatible ARVs. Coating of
Cellets® allows segregation of the drug compounds and the formulation appears to be well tolerated. Extensive characterisation of drug transporters in vaginal and rectal mucosae has identified factors that may influence tissue permeability. Of the drugs investigated in this project, however, dapivirine and tenofovir are likely to transfer across the epithelium in a transporter-independent manner while darunavir may be affected by efflux transporters.

Project Context and Objectives:
The MOTIF project aimed to develop approaches to formulation of anti-retroviral drug (ARV) based microbicides against HIV-1 that optimise the tissue distribution of the drugs and solve the problem of combining physicochemically incompatible drugs in a single formulation. Results from the RING and ASPIRE phase III trials of a vaginal ring containing dapivirine (an inhibitor of HIV reverse transcriptase), showing approximately 30% protection overall and higher protection (37% and 56%, respectively) in women older than 21 who used the ring more frequently, provide a rationale for the development of ARV-based microbicides. To be effective, the active drug component of the microbicidc must penetrate cervicovaginal or colorectal epithelium and enter the sub-mucosal T cells that are targets for primary infection. The MOTIF project also investigated whether drug transporters play a role in the distribution of ARVs in mucosal tissue and whether drug formulations can be modified to optimise such distribution for improved anti-HIV effect.

ARV-based microbicides that combine two or more drugs may be more effective than a single ARV. However, co-formulation of ARVs can be problematic. Previous work by Particle Sciences (a member of the MOTIF consortium) demonstrated a basic incompatibility on co-formulation of two ARVs, darunavir (HIV protease inhibitor) and tenofovir (HIV reverse transcriptase inhibitor) in a single gel. Using these drugs as examples, in the MOTIF project, Particle Sciences investigated approaches that may be widely applicable to co-formulation of ARVs.

Specific objectives of the project were:
1. To investigate expression of drug uptake and efflux transporters in cervicovaginal and colorectal tissue of humans, macaques and rabbits.
2. To develop formulations for combinations of Tenofovir, Darunavir and Dapivirine that are designed to be generally applicable to compounds with incompatible physicochemical properties and to provide optimal drug concentrations at target sites.
3. To develop in vitro model systems for rapid measurement of drug transport that are relevant for vaginally and rectally-delivered microbicides.
4. To define in vitro antiviral activity (against SHIV/HIV) and tissue compatibility of formulated ARV-microbicides in human and rhesus macaque mucosal tissue explants.
5. To perform pharmacokinetic (PK) and pharmacodynamic (PD) studies of microbicide formulations in the rhesus macaque model.
6. To perform ADMET studies of vaginally and rectally administered microbicides in rabbit models.

Project Results:
The main outcomes from the MOTIF project were: i. establishment of generic formulation procedures that allow drugs with incompatible physicochemical properties to be combined in single vehicles; ii. a comprehensive description of drug transporter expression in cervicovaginal and colorectal mucosae and cell lines; iii. definition of the mechanisms by which anti-retroviral drugs (ARVs) representing three different classes transfer across the epithelium; iv. use of tissue explant models to compare efficacy and biocompatibility of ARVs; v. in vivo data in animal models of drug distribution and tolerance.

i. Formulation studies
Responsible partners: B. Frank, M. Mitchnick, Particle Sciences.

Particle Sciences (PSI) participated in WP2, formulation. PSI's overall role was to develop formulations for combinations of active pharmaceutical ingredients (API's) that are designed to be generally applicable to compounds with different and potentially incompatible physicochemical properties, and to provide optimal drug concentrations at target sites. Additionally,
PSI was responsible for making test materials to be used in various non-human primate investigations.

It was the intent of MOTIF WP2 to take a more innovative approach to microbicides formulation than currently accepted formulation approaches, and to focus on the desired delivery profile informed by both existing knowledge and the transporter data gathered in MOTIF. While truly novel excipients were not evaluated, excipients used in other dosage forms (non-vaginal) were considered as options, drastically expanding the formulation/delivery options open to these compounds.

The WP was divided over three years. Broadly, the objectives and timeline are:

- **Objective 1:** 1 – 6 months: Determine solubility’s of the API’s. Perform compatibility studies with the three API’s and relevant excipients
- **Objective 2:** 6 – 24 months: Formulate the three API’s separately and together and demonstrate stability and control over drug release profiles in vitro
- **Objective 3:** 24 – 36 months: Supply WP5 with samples for NHP investigations and continue stability programs started in months 6 – 24.

It should be noted that though the MOTIF project was originally designed and initiated around combinations of three API’s: Darunavir, Dapivirine, and Tenofovir, the work was later amended for non-technical reasons to exclude Dapivirine and concentrate on Darunavir/Tenofovir combinations only.

Analytical methods were leveraged from Particle Sciences’ previous experience working with these compounds. In the anticipation of formulating Dapivirine, Darunavir, and Tenofovir into a stable prototype, the solubilities of Dapivirine, Darunavir, and Tenofovir were assessed by experimental means. The resulting data was modeled using the software HSPiP to determine the Hansen Solubility Parameters (HSPs). During the formulation development phase, these parameters allow for comparison of each active to the parameters of excipients based on the concept “like dissolves like.”

During the assessment, it was found that the HSPs for Dapivirine and Darunavir were similar while those of Tenofovir are unable to be accurately determined, as water solubility is not handled by the program. Unsurprisingly, it was found the Dapivirine and Darunavir were more hydrophobic while Tenofovir was more hydrophilic. Excipient Compatibility information, as well as analytical methods were leveraged from previous work performed using these API’s.

The first stage of formulation development, centered on development of dissolving films as a novel vaginal delivery format. Development of the dissolving film dosage forms resulted in production of both single API and dual API formulations. These formulations were evaluated for stability, dissolution, and supplied to MOTIF collaborators for in-vivo evaluation.

An additional formulation type extensively investigated included inert core particles coated with API using a fluidized bed process. The inert core particles chosen were Cellets® 500 (500-710 µm spherical microcrystalline particles). The Cellets® work entailed coating the microcrystalline core particles with a polymeric binder coat (Opadry®) containing the API. Both API’s were solubilized in the binder coat solution, using methanol for Darunavir and water for Tenofovir.

Example formulations were made of single API coated Cellets®, as well as dual coated versions wherein the API’s were applied successively as separate layers on the core, to minimize interaction and degradation. Additionally, seal-coats of placebo polymer were investigated to further isolate the API’s from each other, as well as to determine the seal-coat’s ability to modulate release of the API’s. Example formulations of several Cellets® based compositions were tested for stability, dissolution, and supplied to MOTIF collaborators for in-vivo evaluation.

Some limited investigational work was also done on Darunavir loaded LyoCells®, a proprietary reverse cubic phase lipid delivery system. This work was initiated as a possible method to bypass the PGP efflux pump effect observed for Darunavir, though these were not ultimately evaluated by the MOTIF team. Spray-drying Darunavir into a polymer matrix was also
Particle Sciences investigated a number of formulation approaches within the scope of the MOTIF program including dissolving films, coated Cellets®, LyoCells® and spray-drying. The dissolving films and coated Cellets® were progressed through preformulation, stability, dissolution and supply of materials for testing by various MOTIF collaborators. From the work performed, both approaches appear as conceptually viable strategies for formulating materials with different and potentially incompatible physicochemical properties. Certainly further modification/optimization could be performed on these approaches, though some of this would necessarily be dictated by the particular nature of the API materials to be delivered.

ii. Drug transporters in cervicovaginal and colorectal mucosae

Responsible partners: K. Hijazi, UNIABDN; C. Cambiaggi, Microbiotec; F. Ianelli, UNISI; R. Le Grand, CEA.

Gene expression of drug transporters which are known to be substrates for several classes of antiretroviral drugs was demonstrated in human cervicovaginal and colorectal tissue. Efflux transporters included P-gp, BCRP and MRP transporters. Uptake transporters included CNT, ENT and OATP transporters. OAT transporters associated with transport of tenofovir were not expressed in either cervicovaginal or colorectal tissue. Expression of drug transporters in colorectal tissue was also confirmed by immunostaining as shown in Fig. 1 (see attached figs and tables document).

We have also described transporters for antiretroviral drugs in macaque and rabbit cervicovaginal and colorectal mucosae and compared gene expression to human cervicovaginal and colorectal mucosae respectively. Overall there were strong similarities in drug transporter expression among human, macaque and rabbit tissue. Comparative gene expression in human, macaque and rabbit tissue is shown in Table 1 (attached).

Expression of transporters for antiretroviral drugs were also demonstrated in colorectal mucosal CD4+ T lymphocytes and compared to circulating α4β7+CD4+ T cells which traffic to the intestine and have been shown to be preferentially infected by HIV-1. As shown in Fig.2 (attached) expression of efflux transporters MRP3, MRP5, BCRP and uptake transporter CNT2 was significantly higher in colorectal CD4+ T cells compared to circulating CD4+ T cells. Conversely, circulating α4β7+CD4+ T cells demonstrated significantly higher expression of OATPD compared to colorectal CD4+ T cells. The qualitative and quantitative differences in drug transporter gene expression profiles between α4β7+CD4+ T cells and total mucosal CD4+ T cells may have significant implications for the efficacy of rectally delivered ARV-microbicides.

Drug transporter expression was investigated in a panel of cervicovaginal and colorectal cell lines to determine their suitability as surrogates of cervicovaginal and colorectal epithelium, respectively, in transport kinetics studies. Comparative analysis of expression on tissue and cell lines revealed that:

- Caco-2 cell lines were the best surrogate of colorectal epithelium.
- No single cervicovaginal cell line proved superior to others in terms of replicating the drug transporter expression profile of cervicovaginal tissues - Expression of efflux ABC transporters in cervical tissue was best represented in HeLa, Ect1/E6E7 and End1/E6E7 cell lines. Expression of influx OCT and ENT transporters in ectocervix matched expression in Hela while expression of influx SLCO transporters in vagina was best reflected in VK2/E6E7 cell line.

To measure the effect of dapivirine, darunavir and tenofovir on drug transporter expression the cell lines detailed above were used as surrogate for colorectal and cervicovaginal mucosae.

Stimulation of Caco-2 with tenofovir dissolving films (~2 mg) produced within WP2 led to significant up-regulation of MRP5, OATPE and LAT2 expression and down-regulation of ENT2 and MRP3. Stimulation of Caco-2 cells with the darunavir dissolving film (~0.28 mg) also produced by our partners in WP2 induced significant up-regulation of BCRP and OATPE genes. Taken together, these data suggest that darunavir-based microbicides incorporating tenofovir may result in drug-drug interactions likely to affect distribution of individual drugs to sub-epithelial target cell in the colorectal mucosae.
Cervicovaginal cell line stimulation with darunavir and dapivirine upregulated MRP transporters, including MRP5 involved in transport of tenofovir (Fig. 3, attached). Dapivirine also significantly downregulated tenofovir substrate MRP4 in cervical cell lines. Treatment with darunavir and dapivirine showed no significant effect on expression of BCRP, MRP2 and P-gp implicated in efflux of different ARV drugs. Darunavir strongly induced expression of CNT3 involved in cell uptake of nucleotide/nucleoside analogue reverse transcriptase inhibitors and SLCO drug transporters involved in cell uptake of protease inhibitors. The modulatory effect of darunavir and dapivirine on expression of drug transporters involved in transport of tenofovir points to the possibility of combining these drugs to improve retention of individual drugs at the cervicovaginal mucosae.

The effect of diverse components of the cervicovaginal environment on expression and activity of drug transporters in cervicovaginal cell lines was investigated. The most prominent expression changes were observed as effect of pro-inflammatory cytokines. Expression of the P-gp gene in VK2/E6E7 cells was induced by 5-fold, 15-fold and 22-fold when cells were stimulated for 72 hours with TNF-α, IL-1β and IL-6, respectively. However, only the upregulatory effect of TNF-α, IL-1β resulted in significant differential P-gp activity as revealed by digoxin accumulation transport studies, while IL-6 showed no effect (Fig. 4, attached).

iii. Permeability of ARVs across epithelial cell models

Responsible partners: B. Forbes, C. Kelly (KCL)

In vitro models of rectal and vaginal barrier epithelium were established using transwell cultures of the human cell lines Caco-2 and HEC-1A, respectively (Fig. 5, attachment). Permeability of dapivirine, darunavir and tenofovir were assessed in both models. As shown in Figs 6 and 7 (attachment), transfer of dapivirine across both epithelial models is by transcellular passive diffusion. The more polar ARV, tenofovir, diffuses by the paracellular route. In the Caco-2 model, darunavir is actively effluxed at the apical surface while transfer across the model vaginal epithelium (HEC-1A) is by transcellular diffusion. Thus only darunavir shows transporter-dependent permeability in rectal epithelium. When combinations of two or all three drugs were included in the assay, no effects on permeability of each drug was observed indicating no drug-drug interactions had occurred.

The physiological relevance of these observations was further investigated by measuring drug permeability in ex vivo models (colorectal mucosae from rat, guinea pig and rabbit). As shown in Fig. 8 (attachment), addition of a P-gp inhibitor (GF120918) significantly inhibits efflux of darunavir at the apical surface of both the Caco-2 cell monolayer and rabbit colorectal mucosa. The data also show that there is no drug-drug interaction between darunavir and tenofovir that modifies tissue permeability.

iv. Tissue explant models for microbicide efficacy and biocompatibility

Responsible partners: R. Shattock, J. Makinde (Imperial)

Drug combinations show improved antiviral activities compared with single drugs

The antiviral activities of unformulated ARVs (PMPA, TMC-120 and DRV) were assessed in in a range of cellular and tissue models. Cellular models assessed include PM-1 CD4+ T cells, and peripheral blood derived dendritic cells. Drug activity in human cervical and colorectal tissue as well as in NHP cervical and colorectal tissue was also assessed. We have also extended this objective to the examination of drug activities in combination. Our results depict a progression from cellular to human and NHP models to make a case for the use of these combinations in microbicide formulations. Initial experimental data to determine the viral and drug kinetics in macaque tissue show that combinations of drugs were better able to inhibit viral infection than single drugs.

Biocompatibility profiles of antiretroviral drugs varied between tissue explant models

Biocompatibility studies of drug combinations on human cervical and rectal tissue show differential effect on tissue immune profiles. Cervicovaginal tissue incubation with all drug combinations resulted in no major change to tissue immunological profile whilst rectal tissue incubation with drug combinations resulted in some change to the inflammatory and
chemoattractant (IL-6, IL-8 and P-Selectin) properties of the tissue. Our results underscore the need for rigorous testing of formulated microbicides when available to determine whether similar effects are observed.

Drug transport inhibitors present in mucosal tissue can be targeted to boost the antiviral activities of microbicides. Lastly in cellular (PBMC) and macaque tissue models, we have been able to show that the addition of inhibitors of efflux transporters can boost the antiviral activities of the drugs alone or in combination.

v. Non-human primate and rabbit testing of drug distribution and tolerance
Responsible partners: Roger Le Grand, CEA; Dominik Dostál, MediTox.

Dissolving film and Cellets® formulations of darunavir and tenofovir were tested in vaginal and rectal tolerance studies in rabbits with single or repeat administration of drugs. The formulations were well tolerated. Extensive PK studies of the film formulation were performed in non-human primate models. Analysis of data from determination of drug concentrations in tissue and plasma continues.

Potential Impact:
Impact
This project contributed to impacts as foreseen in the call for proposals as below:

1. Significant contribution to prevention of poverty related diseases by addressing gaps and providing innovative strategies for integrating the inputs of individual research teams.
   Gaps in formulation technology for incorporation into a single vehicle of drugs with widely different physicochemical properties were addressed in this project. Research conducted by Particle Sciences Inc (SME partner) incorporated novel formulation excipients and developed two strategies for formulation that maintain segregation of the drugs within single vehicles, namely dissolving films and Cellets®. Testing of these formulations in PK and tolerance studies provided added value. As one of the world-leading microbicide formulation companies, Particle Sciences is well-positioned to use these novel formulation strategies in the development of microbicides based on combinations of ARVs.

   A further gap that has been extensively addressed in this study was determination of factors that influence drug permeability following topical application at vaginal or rectal mucosal surfaces. Comprehensive investigation of the expression of drug transporter proteins at these mucosae in humans as well as animal models used in microbicide development has provided a rationale for inclusion of compounds to modulate such transporters in microbicide formulations. While inclusion of inhibitors of efflux transporters may contribute to increased uptake of darunavir, the results of the MOTIF project also indicate that for some ARVs (tenofovir, dapivirine) permeability is transporter-independent and formulations should facilitate diffusion by paracellular or transcellular routes.

2. Encouraging SME efforts towards research and innovation.
   Funding provided by the European Union allowed Particle Sciences to perform extensive research into determination of solubility parameters of the ARVs used in this project and selection of formulation excipients as well as design and testing of formulations as described in the Periodic Reports. Funds provided to Microbiotec srl (beneficiary 4) encouraged development of PCR array and transcriptome technologies that were used for investigation and modulation of drug transporter expression. Finally MediTox (beneficiary 3) developed expertise in administration and testing of novel microbicide formulations.

3. Development of broadly applicable formulation strategy.
   The Cellets® formulation developed in this project provides a platform technology for inclusion of active pharmaceutical ingredients (APIs) without regard to API/API incompatibility and should therefore be of use in co-formulation of a variety of drugs for other conditions as well as for other routes of administration.

4. Translation into ... reducing future disease incidence
Improved knowledge of the mechanisms that determine drug distribution in vaginal and rectal mucosae is anticipated to influence formulation and dosing strategies for microbicides. The generic approach developed in this project to co-formulation of combinations of drugs with widely differing properties can be expected to expedite testing of novel microbicide combinations. Combinations identified as promising by the approaches used in this project can then be re-formulated if required for further development. Together, these aspects of the MOTIF project should contribute to development of improved microbicides that deliver optimal levels of drug to target sites of infection. Although the number of new infections is gradually decreasing, the need for effective microbicides is underlined by the most recent WHO/UNAIDS report (2015) that estimates approximately 2 million people were infected in 2014.

Main Dissemination Activities

The dissemination actions in MOTIF were envisaged to disseminate the activities carried out during the entire duration of the project, the main project scientific achievements and the initiatives organised by the partners of the project within the framework of MOTIF as well as their participation in major European and worldwide events and scientific conferences. These activities were led by the dissemination partner, Minerva

Major objectives were

1. To create a dedicated website for MOTIF project, with public and Members’ Only sections
2. To disseminate the activities and results of the project.
3. To increase project awareness via the use of informational and promotional materials (brochures, leaflets etc.) in workshops or conferences in which MOTIF will participate.

MOTIF adopted high impact dissemination actions through efficient and effective communication methods and was able to reach the goals and objectives of the project.

The following tools were developed to facilitate the communication and dissemination actions for the activities.

1. Project Logo
2. Project Leaflet
3. Roll up
4. Project Electronic newsletter
5. Press Releases
6. Project power point template
7. Social Media (Facebook and Twitter) and other online tools
8. Project Video

Within the framework of the communication activities, some media activities were also implemented. Indeed a media list of contacts was drafted and regularly updated, including relevant contacts from the media at national, European and international level that can be interested in the project topics (1 level) and those that are interested in research topic in general (2 level).

Press releases
During the first year and a half of the project 4 press releases were prepared for promoting the project news through European and extra European channels. This is the main form of contacting the media and informing them of what is developing within the MOTIF programme.

The 2 first press releases, prepared in M1, gave brief details about the project and technical details about the starting and ending date, as well as the names of the partners involved; the content of each of them was the launch of the website and the
project kick off meeting.

They were addressed to the main European websites and platforms that promote European projects (Cordis, EU agenda...) and send out to national (mainly in the partners’ countries) and international level.

Another 2 press releases were prepared and spread to major media channels about the annual meeting of the partners in Fontenay-aux-Roses (Paris) and the activities developed during the first year of the project.

In the second half of the project, 2 further press releases were sent describing results produced by some of the MOTIF partners.

The full list of press releases:
• October 1st, 2012 - Launch of Motif Website
• October 24th, 2012 - Motif project Kick off Meeting - Fontenay aux-Roses, France
• March 21st, 2013 - Interview with Robin Shattock interview
• October 21st, 2013 - Identified Candidates Drug Transporters and Microbicides for the Prevention of HIV Infection
• November 18th, 2013 - Potential drug transporters and Microbicides for the Prevention of HIV
• October 30th, 2014 - Getting closer: Identifying drug transporters

All the press releases were written by MINERVA and submitted for review and approval to the DC. Some press releases were translated in other languages and sent to the related local journalists. All of them are available in the “Newsroom” section of the project website, for further accessibility for media or any other interested parties.

Social Media and other online tools
The use of social media is of critical importance in this technology age, therefore, Facebook and Twitter have been used to disseminate MOTIF news as well other news relating to HIV, AIDS, or Microbicide news and other related developments that may be of relevance or interest to MOTIF partners and its affiliates.

MINERVA created the MOTIF Facebook page and MOTIF Twitter account whose direct access was added on the right column of the website with a live Twitter column and Facebook, showing the on-going news. The creation of these pages allowed broader exchange and dissemination of information and the possibility of linking with specific stakeholders interested in the topics of MOTIF.

The Social Media pages were updated with news about the project and other relevant HIV/microbicides topics and interaction with other pages was implemented through the posting of MOTIF news on other profiles, through “like” actions and “retweeting”.

News of particular significance were also posted in the “News” section of the MOTIF website and daily news can all be found on the social media sites.
All partners were requested to “like” the Facebook page and follow the MOTIF Twitter so that they could remain updated on the news posted by MINERVA.

Project Video
A project video was created by MINERVA to be used as an audio-visual promotional tool of MOTIF and its objectives. The video features interviews from each partner, which were shot on October/November 2013, who explain in detail their role in the project, the research they are bringing on and the results achieved so far.
The video also aims to facilitate the comprehension of the research aspects for the public at large and thus be a widely used awareness tool. Final video contents and format were approved by the DC to ensure the video meets requested objectives and displays allowed information in an accurate manner.

The project video was placed to appear in a prominent manner on the opening page of the MOTIF website so that visitors may immediately see the video; it was also posted on the project Facebook and announced on the project Twitter several times.

It can also be seen in youtube following the next link: https://www.youtube.com/watch?v=epYvP88qoWw

Creation and management of MOTIF Website
MINERVA set-up a project website that was launched in December 2012.
The website is accessible through this link: www.motifproject.eu
The MOTIF website has been designed by MINERVA and structured in a way to be clearly accessible by project partners, European Commission officers, interested stakeholders and other general visitors. The Motif website has a top menu divided into 6 sections:
• “Welcome” section, with a small summary of the project, and an explanatory video of it, as well as some testimonials from the partners.
• “Project” presenting the project with inside section “Project Summary”, “Work packages” and “Objectives and Expected results”.
• “Partners”, which contains information about the partners profiles, their work category and the links to the partners websites.
• “Research”, where it’s explained what microbicides are and how do they work. It also includes a section of scientific publications, a glossary of terms and a links page with information related to HIV/AIDS, microbicides and organizations active in this area.
• “Newsroom” section is dedicated to collect information about MOTIF news, events, newsletters, a video and photo gallery and a communication material section (leaflets, posters...).
• “Contact us”

Direct access to the MOTIF Facebook page and a live Twitter wall were added on the right column of the MOTIF website, showing the on-going news. Features of the website are shown in the attachment.

Workshop, 18th June 2015, Brussels, Belgium
A joint workshop was held at the NH Atlanta Hotel in Brussels, Belgium on the 18th June 2015, between MOTIF, CHAARM and AIM-HIV projects to discuss the progression of compounds developed within CHAARM and current results from MOTIF and AIM-HIV projects, The meeting included presentations by Alessandra Martini from the European Commission who discussed Horizon 2020, Julie Fox from KCL and Mitzy Gafos from UCL, who presented the results from current HIV clinical trials, and Wendy Blanda from IMP who spoke about the current microbide projects being funded by IPM. Ole Olesen from EDCTP, Angela Wittelsberger from IMI discussed current and future funding possibilities. Presentations were given about the development, formulation and challenge studies of 3 compounds within CHAARM, DAPIDAR (Dapivirine and Darunavir), UAMC-0138 and J3. The meeting closed with a discussion led by Robin Shattock from Imperial College about the future directions of microbicide research.

List of Websites:
www.motifproject.eu

Project Coordinator:
Professor Charles Kelly
Investigation of Novel Drug Formulations Against HIV

Related information

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