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| Minutes SIOPE Europe Clinical Trials Meeting | |
| Date: Monday 15 October 2007 | Location: ECCO office Brussels, Belgium |
| Chairs: Andrea Biondi (Italy) & Kathy Pritchard-Jones (UK) | |
| Distribution list: Clinical Trials members SIOPE and Michel Ballieu (ECCO) | |

The meeting was opened by Kathy Pritchard-Jones who welcomed everyone to the meeting. Together with Andrea Biondi she explained that the purpose of the meeting is to inform the clinical trials group with an update on the opening of the new SIOPE office as part of the ECCO offices and the start up of the Clinical Trials helpdesk. Also the feedback from EMEA/European Commission meeting held on Oct 3rd on the Operation of the EU CTD and implications for non-commercial clinical trials.

1. Goals and objectives for Clinical Trials SIOPE (Kathy Pritchard-Jones)

The aim of SIOPE Europe is to “assure the best possible care and outcome for all children and young people with cancer in Europe”. And this will be achieved by promoting the following objectives and goals by each one of the members.

- Comprehensive cancer registration
- Encouraging a maximum recruitment to clinical trials
- Facilitating basic research
- Setting standards for professional education
- Working in partnership with parents and patients
- Lobbying governments and other to ensure appropriate resources are available

2. Update on SIOPE activities and Introduction of new office staff

2.1 SIOPE Europe (Andrea Biondi)

- SIOPE is proud to announce the opening of the **SIOPE Europe office** which is incorporated and located in the ECCO offices in Brussels. This partnership with ECCO will allow SIOPE to have a very close and strong relationship as ECCO is a strong umbrella organization which will allow SIOPE to have access to several current and future plans/initiatives
- **Two new SIOPE staff members** (50% SIOPE and 50% ECCO)
 - Samira Essiaf: Scientific Coordinator
 - Jocelyne Wang: membership and website administrator
- Start up by Samira Essiaf of **EU Clinical Trials support desk** specific to needs of pediatric haem/onc in progress.

2.2 Revised statutes & membership (Andrea Biondi)

The current **statutes** need to be reviewed:

- As the **office is moving** to ECCO so it needs to be legally constituted under Belgian law.
- **Name of the organization:** Board prefers to retain SIOPE Europe (acronym SIOPE) but a new logo has to be designed.
- New **membership:** Mandate given to the SIOPE Board at AGM (Barcelona) to negotiate new membership categories and to finalize the revised statutes.

2.3 SIOPE Membership (Kathy Pritchard-Jones)

The SIOPE membership voting and different type conditions have been explained and will be incorporated in the statutes that are currently in a review process.

- **Voting membership** open to any person or legal entity that:
 - Is resident or has its office in Europe
 - Supports the goals of the organization
 - Has been approved by the Board of Directors in accordance with specified rules (By-laws)
 - Meets the criteria for one of the categories of voting membership
- **Full members**
 - Member of SIOPE (International)
 - A legal entity that represents or is composed of persons engaged in a professional capacity in clinical cancer care or research in childhood or adolescence
- **Associate members**
 - Any unincorporated body of physical persons, including but not limited to, Working or Study groups, which meet any criteria described in the internal rules of the association and
 - Are active in an area of significant concern either to:
 - Persons working in a professional capacity in childhood/adolescent cancer care or research, or
 - Children or adolescents being treated for cancer or their families
- In addition the update of the SIOPE Membership: There are **No Membership fees** planned

3. Introduction to FECS new CEO, Michel Ballieu and update on plans for new structure of ECCO (European Cancer Organization (Michel Ballieu))

Michel Ballieu introduced **ECCO** to the SIOPE clinical trials team and explained the change of the name from FECS into ECCO as well the structural organization including the integration of the SIOPE office and aim and role of ECCO.

- **Aim:** ECCO would like to put the **patient back in the centre** as the patient needs the best treatment and care in Europe. And secondly coordinate the **interaction** between a **maximum number of organizations**.
- **Organization ECCO:** **SIOPE** is a **Founding member** of the ECCO organization and benefits from several privileges such as the conferences, special rates, secretariat, communication, voting right, annual member meeting and financially.
- **Integration of the SIOPE office into the ECCO office:** Purpose of this integration is firstly because of the **reduced costs** (no investment in new infrastructure or material as it is already provided by ECCO) and secondly beneficial as **back up for the SIOPE staff members** and for **exchange** of information and **experience with ECCO staff**.

4. **SIOPE: Initial and subsequent Priorities and achievements (Kathy Pritchard-Jones)**

As described in the position paper of June 2006 the **initial priorities** for SIOPE are to **facilitate clinical Trials** and to **provide common:**

- Interface for **information exchange**
- Voice for **communicating with the regulators**
- **Link to EU initiatives** under “**Medicines for children**”

Now in addition to the above indicated initial priorities the following **subsequent priorities** have been setup to:

- **Develop** the “**best practice**” **standards for treatment of the main childhood cancers** which may help with avoiding the IMP categorization.
- **Develop** common **standards for design and implementation of clinical trials**
- **Provide education and training building on the existing standard curriculum** that was **developed by SIOPE**

At this moment the **SIOPE Clinical Trials “committee”** has **succeeded** the following achievements.

- The **organization of 2 meetings of representatives** (May 05 and Sep 06) of
 - National childhood organizations
 - Multinational clinical trial group
 - Parents group in Europe
- **Mandate to speak with one voice on behalf of the pediatric hematology-oncology** (professionals and parents/patients) in **Europe with potential funders (DG Research/FP7) and Regulators (EMEA, European Commission)**
- **SIOPE coordinated responses to the EMEA consultations**
 - Pediatric **priority drugs list**, led to inclusion of additional drugs on the list which is essential to **facilitate applications for FP7** funding under the call for “development of off-patent medicines for children”. And **worked with TEDDY** recognized as oncology expert group
 - **Ethics of clinical trials in children**
 - **Pediatric “network of networks”**
- **SIOPE coordinated responses to the EC/Clinical Trial Facilitations Group (CTFG) consultations**
 - First **submission** occurred **September 2005**
 - **Further submissions** in response to public consultations on specific aspects of **EU CTD for non-commercial trials** - Sept/Oct 2006
 - **Hope for positive changes** following the meeting coordinated by the **EMEA** for the **EU Commission on 3rd Oct 2007**
 - **Dialogue** now **established** with **SIOPE recognized** as an **important voice** for **pediatric clinical trials** representing experienced trial groups

- **Key points from EMEA-EC meeting on 3rd Oct 2007**
 - **Disagreement** between regulators & researchers regarding need for **revision of the EU CTD**
>> Commissioners recognized this and were listening to the researchers
 - **Much** (successful) experience of trial group structures that meet current requirements
 - **Excessive bureaucracy** has been clearly indicated
 - **Ongoing issues** (especially for pediatrics):
 - IMPs and pharmacovigilance especially in phase III trials
 - Pan-European sponsorship
 - National variations in interpretation especially
 - Indemnity and insurance costs
 - Free drug supplies
 - Recognition of co-sponsor structure and other
 - *Comments from and to the SIOPE Clinical Trials team:*
 - Every group should be lobbying as there is a window of opportunity to influence a decision about revising the Directive.
 - It is very important to involve the parents and patients group as they have the most influence on politicians.

>> Actions and Key Issues

- A **letter** with a **clear but simple explanation** in regards to the EU lobbying should be drafted and send to the parents groups asking them to lobby at national and European level.
- **Harmonization** needs to be improved and standardized at the easiest level compatible with good clinical practice.
Variation in the interpretation of the **definition of IMPs** has had a particularly negative bureaucratic impact on clinical trials in children, where many marketed drugs are used off label.

5. SIOPE has facilitated two applications for FP7 funding for clinical trials of off-patent medicines in children (Submitted to Sept 2007 call)

1. **EPOC** (Alan Boddy, Newcastle University, UK)
 - European Pediatric oncology Off-patent medicine Consortium - in depth study of 4 drugs (Act D, Cyclophosphamide, Doxorubicin, Vincristine)
2. **O3K** (Gilles Vassal, IGR, France)
 - Oral formulation of cyclophosphamide and temozolamide

6. ERA-Net Plus Action for SIOPE (Ruth Ladenstein)

Ruth Ladenstein introduced and explained the ERA-Net and the ERA-Net plus Action to the SIOPE CT trials group to see if there is a need and if it is feasible for SIOPE to participate into this program

ERA-Nets belong to „coordination and support actions“ of the FP7:

- For the **coordination** and **mutual opening** of **national research programs** and as well open “bottom-up” **approach** to **all areas of research**
- To **establish cooperation** between **national programs** leading to **joint transnational research programs**
- **Initiative rests** with **member states/organizations**
- Main task: **Organization** of **transnational calls** for **research proposals**(> 5 M€)

The **ERA-Nets are open to Program owners** (National ministries/regional authorities), **Program managers** (National funding institutions) and **other legal entities** (charities and societies). And for the participation into the ERA-Net program the following **minimum requirements** are needed:

- At least **5 program owners/managers** from **5 different countries**
- **Approx. 4 M € committed by program owners/managers**
- **Management and organizational structure**
- **Topic** (Pediatric Oncology) **NOT covered by existing ERA-Net**
- **Next 2-step call for ERA-Net** is expected with **deadline for June 2008**

Now what is the difference between ERA-Net and the ERA-Net Plus?

ERA-Net:

- Funds from national funding bodies are redistributed nationally
- Funds from EC cover management and administration costs
- Only researchers from participating nations are funded

ERA-Net Plus:

- Funds from national funding bodies are redistributed without consideration for their origin
- National funds are topped up (25%-30%) by the EC + M&A costs
- Only researchers from participating nations are funded

Enrollment requirements and Timelines

>> How to proceed with the implementation of an SIOPE-ERA-Net?

- **Commitment of SIOPE Europe** to proceed with the **identification** of proposal **coordinator** and **national representatives**
- **Develop** written **concept**
- **Contact** of **national program owners/managers** for **negotiations**
- **Collecting** about **4 M€ of financial commitment**
- **Financial commitment** for ERA-Net Plus **without national redistribution**
- Submit **proposal in June 2008**

>> The Timelines

- **November 2007:** Seek national **agreement and commitment** of national coordinators/representatives/groups till November 2007 proposal **coordinator** and **national**
- **November to December 2007:** Develop **written concept**
- **December 2007:** **Contact** of **national program owners/managers** for **negotiations**
- **January March 2008:** Collecting about **4 M€ of financial commitment**
- **April- Mai 2008:** **Finalization** of the **proposal**
- **June 2008:** **Submission** of the **proposal**

Action Points: *Follow up on the need and feasibility of SIOPE to participate into the ERA-Net Plus program. Ruth Ladenstein to present at the next SIOPE Europe Board meeting in Mumbai*

7. **FL07-01 Investigator Driven Clinical Trials Workplan (IDCT) (Stefan Bielack)**

Stefan Bielack presented the Investigator Driven Clinical Trials Work plan (IDCT) initiative of the European Science Foundation. He explained that the goal of this activity is to **create recommendations** on how to **better coordinate various national and European Clinical Trials initiatives** which will lead to a consensus conference that will take place in Brussels on the 10-11 July 2008.

Now towards this goal **5 workshops** will be organized early next year to address:

1. Categories and Design of Clinical Trials
2. Regulatory and Legal issues, IPR and Data Sharing
3. Funding and Models of Partnerships
4. Management and Logistics of Investigator-Driven Clinical Trials
5. Education, Training, Career and Authorship.

He urged participants to look at the website and to engage in the process.

<http://www.esf.org/activities/forward-looks/medical-sciences-emrc/fl-07-01-investigator-driven-clinical-trials.html>

8. **SIOPE Logo on Clinical Trials (Ruth Ladenstein)**

Can the logo “SIOPE” (SIOPE) constitute any sort of **liability for SIOPE**, especially in view of the liability of a sponsor in a clinical trial, is the **question** that Ruth Ladenstein has been investigating with a **group of lawyers**. The outcome of the lawyer team resulted in some of the following statements so therefore it would be advisable to use the expertise of the EORTC who has a lot of experience in this domain.

- The use of the association (study group) logo “SIOPE” **does not result in any special liability** regarding sponsor responsibilities for the association or study group providing the sponsor is clearly identified.
- **If the sponsor is not clearly identified** in the trial protocol, **the use of the logo “SIOPE” may create the impression that SIOPE assumes the overall responsibility** for the implementation of the trial and could be addressed for claims in this matter.

9. **Clinical Trials Action points (Future) and Issues (Kathy Pritchard-Jones)**

The **action points** of the **SIOPE clinical trials** group:

1. The **Clinical Trials group** and national childhood cancer organizations should forward their **needs** to the **SIOPE scientific coordinator Samira Essiaf**. So that this can all be centralized and from there a **SIOPE central functioning Clinical trials helpdesk (network)** can be **created and maintained**.
2. The **development of a common platform** for
 - **Trial design** and implementation (Maria Grazia Valsecchi)
 - **Best practice guidelines**
 - **GCP training** resource specific to needs of pediatrics
3. Looking in to the possibilities **to link initiatives within ECCO**
4. **Maintenance** of the **Membership database** and **updates on the European activities** via for example a Newsletter and other.
5. Exploit pediatric program within ECCO congress

- Enhance ongoing Education and Training activities
- Useful meeting point for clinical trials groups
- Enhances SIOPE finances

The **Clinical Trials Issues** that the **SIOPE clinical trials** group is currently facing are:

1. Sponsor ship
2. Legal liability of the "SIOPE" logo
3. Is there a need for SIOPE endorsement to access national resources
4. Is the long term goal of single platform desirable and achievable

10. Close out and Follow up Actions

- Feedback on the **EU lobbying** will be communicated to the Clinical Trials team as soon as this has been obtained
- **Website**
 - >> Agreement needed on **accessibility** on members and clinical trials documentation
 - >> Creation of the **News Letter** by Samira Essiaf and Jocelyne Wang
- Start up of the **Clinical Trials helpdesk** (network) by Samira Essiaf
 - >> **Input and help** from all members would be **much appreciated** so that the **needs** for all members **can be achieved**
- **Education**
 - >> ECCO organizes a Workshop called Flims 10 which is a workshop on "Methods in Clinical Cancer Research (21-27 June 2008)"
- Agreement on the participation and enrollment to the **Era-Net plus project**
- **Finalization** on the SIOPE **statutes**