Prevention of over-volunteering in Europe: "How to get a European-wide acceptable system going?"

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Conflict of interest

No grants received from any company mentioned in this presentation

Presentation is non-commercial and the author always controlled the content of the slides

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Agenda

Framing the landscape of study volunteering

Frequency
Types
Location

Central Register Databases in Europe

Observations on registration and registers

Proposal going forward

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Frequency of Volunteering

Guidelines for Phase 1 Clinical trials (abpi)

Subjects must neither:

- Take part > one trial at a time
- Receive > 10 milliSievert of radioactivity in any 12-month period
- In general, subjects should not receive an IMP systemically < 3 months after the previous one

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### Studies with Healthy Volunteers

<table>
<thead>
<tr>
<th>Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I studies</td>
</tr>
<tr>
<td>Phase II studies with healthy volunteers as comparator</td>
</tr>
<tr>
<td>Vaccination studies</td>
</tr>
<tr>
<td>Device studies</td>
</tr>
<tr>
<td>Studies with a diet</td>
</tr>
<tr>
<td>Investigator driven studies (academia)</td>
</tr>
<tr>
<td>Observational studies</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Where</th>
<th>Phase 1 units</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospital departments</td>
</tr>
<tr>
<td></td>
<td>Vaccination centres</td>
</tr>
</tbody>
</table>
### Volunteer temptations

<table>
<thead>
<tr>
<th>Why participate?</th>
<th>Payment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Travel reimbursement</td>
</tr>
<tr>
<td></td>
<td>Internet information: where, payment</td>
</tr>
</tbody>
</table>
Number of participating Healthy Volunteers

• 816 STUDIES 2016 (Clinicaltrials.gov)

• > 28,500 SUBJECTS/YEAR
Central Register Database

2 databases used

1 database used

1 database used

No databases used
United Kingdom

TOPs

• 2013 Health Research Authority
• MHRA accreditation - IRB approval
• Insurance number/passport & nationality
• Web-based
• Free

NVR

• Open access database of 1 commercial site
• Web-based
• Free
VRB

- French Ministry of Health
- Mandatory 1988
- Compensation
- Social security number + initials
- Web-based
- Free
Belgium – Germany - Netherlands

VIPCHECK

- Privately owned
- Data ID
- Payment
- Not web based
- Bad support
- Not used by all sites
- Future?
Central Register Database

No databases used

?? Subjects ??
Bridging studies

Bridging studies with Japanese HV
Central Register HV Databases in Europe

Conclusion: French & UK people should stay in their country

- No waterproof system in Germany, The Netherlands, Belgium
- Existing systems not used by all institutions
- No system in other European countries
- They do not prevent simultaneous and multi participation

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### Ethical, Legal & Medical Concerns

<table>
<thead>
<tr>
<th>Concerns</th>
<th>Possibility of unknown interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Possibility of contaminated study parameters</td>
</tr>
<tr>
<td></td>
<td>Uncontrolled radiation exposure</td>
</tr>
<tr>
<td></td>
<td>Unknown consequences for the research subjects</td>
</tr>
<tr>
<td></td>
<td>Loss of insurance coverage for research subjects</td>
</tr>
</tbody>
</table>
## Working Group: User Requirements

<table>
<thead>
<tr>
<th>Country</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Netherlands</td>
<td>PRA (A. Kamps &amp; R. Nijssen)</td>
</tr>
<tr>
<td></td>
<td>CHDR (E. Jonxis)</td>
</tr>
<tr>
<td></td>
<td>QPS (I. Den Daas)</td>
</tr>
<tr>
<td>Germany</td>
<td>B.I. (P. Liedl &amp; M. Manzoni)</td>
</tr>
<tr>
<td>Belgium</td>
<td>SGS (K. Vermeiren &amp; L. Janssen)</td>
</tr>
<tr>
<td></td>
<td>JnJ (G. Hasting)</td>
</tr>
<tr>
<td></td>
<td>Pfizer (C. Meganck &amp; D. Malisse)</td>
</tr>
<tr>
<td></td>
<td>Research Aalst (A. Peremans)</td>
</tr>
</tbody>
</table>
## Other Databases

<table>
<thead>
<tr>
<th><strong>EUROPE</strong></th>
<th><strong>US</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>DUPCheck</td>
<td>Verified Clinical Trials</td>
</tr>
<tr>
<td>CNS Phase II, III</td>
<td>Phase I, II, III</td>
</tr>
<tr>
<td>Request by pharmaceutical companies</td>
<td>Used by pharmaceutical companies</td>
</tr>
<tr>
<td>Expansion possible to Phase I</td>
<td>VCT: Willing to expand to Europe</td>
</tr>
</tbody>
</table>

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### Global European Subject Database

**Requirements:**

- Mandatory for all institutions in Europe including healthy volunteers

<table>
<thead>
<tr>
<th>Unique subject identifier</th>
<th>Sex + birthdate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Different options</td>
</tr>
<tr>
<td></td>
<td>Finger print / iris scan?</td>
</tr>
</tbody>
</table>

- Web-based

- Dealing with language specific characters

- Proof of verification (reports) – review by Pharmaceutical Companies
Global European Subject Database

Requirements:

- Standardized procedures
- User friendly and not time consuming
- Confidentiality – Data Protection Laws
- Support
- Also patients?
Options for the future
EMA

- Make one of the existing databases mandatory for European studies / create new database

(Draft Guideline FIH studies) Concomitant exposure of subjects to IMPs across trials, consideration may be given to trial sites participation in e.g; national initiatives to prevent over-volunteering, where available
Option 2

EUFEMED

- PSSS (non-commercial approach)
- Development necessities
- Maintenance & Support costs
Option 3

Centralised database

Owned by EMA?
EUFEMED?

User Interface Product

TOPs, VRB, DUPCheck, VCT ...
EDC systems
Option 4

Pharmaceutical Companies

• Make register in a database mandatory for their studies
• Uncontaminated study parameters
• Naïve study population
• Safety subjects
Overall Conclusion

Conclusion:

Need for European regulation and legislation on participation of Healthy Volunteers in all types of clinical trials in Europe

Need for central European Subject Database

Raise the ethical standards and safety of clinical research in Europe to a higher level
March 13, 2006

Revision European guidelines for FIH phase I clinical trials

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Updated EMA Guideline on strategy to identify and mitigate risks for FIH and early clinical trials with investigational medicinal products
European Database Mandatory
QUESTIONS AND ANSWERS