

MANAGING OPERATION PROCEDURES IN COLLABORATIVE PROJECTS

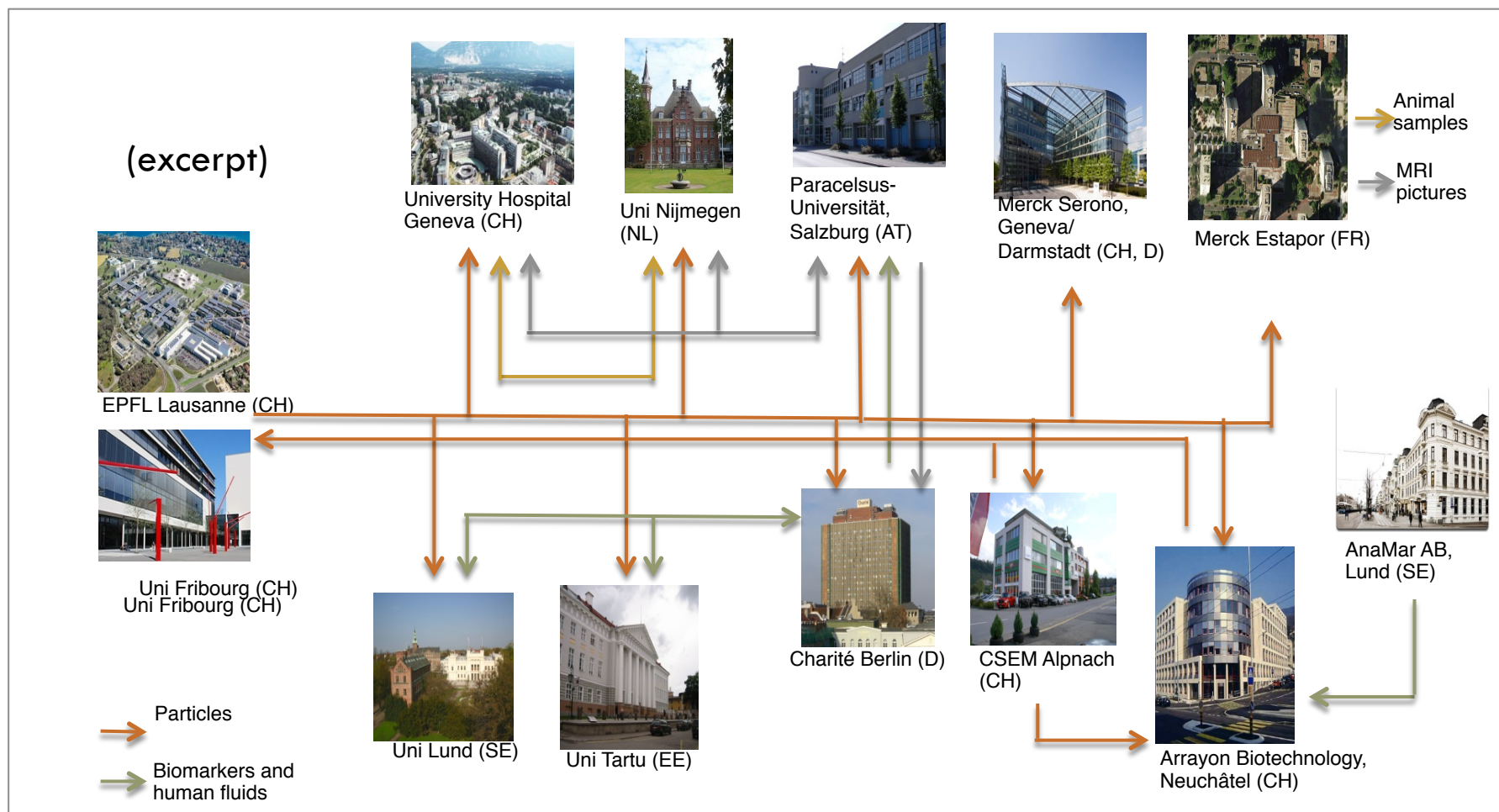
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Introduction

- NanoDiaRA: development of nanoparticles and biomarkers for early *in vivo* diagnosis of inflammatory diseases.
- 15 partners, using NPs in biology, biotechnology, medicine, physics and microtechnology.
- Requirements: transparency and reproducibility of the scientific and technological outcome in the different research fields.
- Challenge with Nanotoxicology: it's a non-regulated area, not all methods are established.

Sample exchange in NanoDiaRA



How to meet the challenges?

- What such a consortium need is an easy solution, a combined answer
 - ▣ Lab scale → Standard Operating Procedures (SOPs) and their management
 - ▣ Project level → Electronic Sample Book (ESB)

Lab book

- Purpose:
 - ▣ Organizational tool
 - ▣ Memory aid
 - ▣ Documentation for Intellectual property (IP) questions



Lab book



8/27/08

OPERON-LIKE ORGANIZATION OF THE GAL GENES

Although eukaryotes lack true operons, there are examples of operon-like gene clusters. Three examples are the galactose utilization genes in *S. cerevisiae* (*GAL1, GAL10, GAL7*), the allantoin degradation genes in *S. G.* (*DAL1, DAL2, DAL3, DAL4, DCG1*), and the thiaminol synthesis genes in *Arabidopsis* (*THA5, THA4, THA3*):



Two explanations have been given to account for this organization: genetic linkage and metabolic channeling.

The genetic linkage hypothesis seems to be favored in the literature. It is interesting to note, however, that all three pathways above have intermediates that are toxic to the organism (in red). Here I want to test the hypothesis that the operon-like organization allows for better co-regulation of the genes and helps ~~channel~~ maintain flux through the pathway thus prevent the accumulation of the toxic intermediate →

Lab book

- Often left aside, filled up weeks after the experiment → Prepare an explicative SOP
 - Lack of information:
 - ▣ Explanation of the experiment purpose missing.
 - ▣ Figures missing titles, axis description.
 - ▣ Troubleshooting: even little details make the difference.
 - ▣ Conclusions: need to plan future experiments.
- Lab book should be checked and signed every week by supervisors.
- Use of SOPs

SOPs

Standard Operating Procedures

*SOPs tell people what to do, and how to do it**

*Edy V and Gamlen M 1994 Standard Operating Procedures *Good Clinical, Laboratory and Manufacturing Practices: Techniques for the QA Professional* ed Carson P and Dent N (Cambridge: The Royal Society of Chemistry) chapter 27 pp 387-398.

SOPs: Why?


- Part of control process
- Protocols are present in labs, but always with different version, people have their own recipes
- Collaborators may have broad background from different fields
- In collaborative projects: physical distance

SOPs: Content


- Contain a quick description of the procedure
- Material (consumables, chemicals) and equipment used
- Method with a clear walk-through without too much details
- Adaptation for different use (ex: for *in vivo* proceed ..., for *in vitro*...)
- Picture may be included for better understanding

SOPs: Template

- Naming: Type, number, version, title
- Author and responsible person
- When does the document become effective?
- Replaces other document?
- Summary
- Used Materials
- Step by step procedure



NanoDiaRA
Particles, Molecules & Cells · Diagnosis in-vitro
& in-vivo · Rheumatoid Arthritis & Osteoarthritis



EPFL
ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

TITLE DRAFT

	Function	Name	Date / Signature
Author	Document control	Marie-Gabrielle Beuzelin Olivier	
Approvals	Director LTP	Pr Heinrich Hofmann	

SOP No.	SOPS PR x-yD
Becomes effective on	
Document being replaced	Previous version from date by initials

SUMMARY
This following protocol describes

MATERIALS REQUIRED

INSTRUMENTS
1. xx
2. oo (Brand, product number)

CONSUMABLES
Consult latest "List of lab material" spreadsheet for current or alternative suppliers and part numbers.
1. Required consumables (Brand, product number)
2. Chemicals purity (Brand, product number)

SOLUTIONS AND BUFFERS

Conc. solution name (for volume mL)
1. In a suitable vessel add the following :
 a. powder x mL
 b. diluent y mL
 2. Stir to mix.
 3. Other details

METHOD

NOTES
~~General important recommendations.~~

TITLE
~~sub title~~
1. Description of the methods steps B la ...

TITLE
1. Other step description of the process

APPENDIX
Additional informations useful for the procedure

SOP No: SOPS PR x-yD
Page 1 of 1

SOPs: Requirements

- Protected document: only the final version is available
- Copies allowed but restricted and mentioned
- Version must change when modifications are necessary, versioning system should be established

SOPs: Requirements in collaborations

- Accessible to all partners
- Reproducible
- Same SOPs for same procedures
- Allocation to samples and probes
- Comparable results

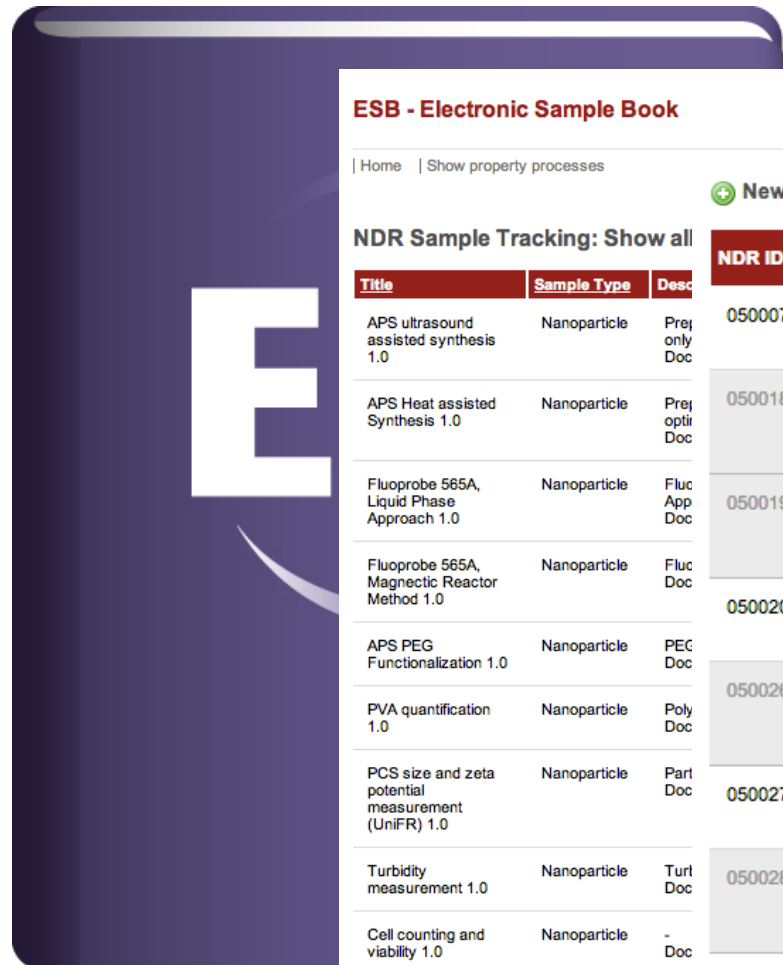
Electronic sample book



Electronic Sample Book

- Sample record and tracking
 - ▣ Sample analysis
 - ▣ Ranges of acceptance
 - ▣ Certificates of Analysis, result sheets and other accompanying documents
 - ▣ Complete tracking of probes
- Exchange of results and protocols
 - ▣ Tests performed
 - ▣ Procedures
 - ▣ Results obtained

Electronic sample book



ESB - Electronic Sample Book

| Home | Show property processes


[+ New Sample](#)

NDR Sample Tracking: Show all


Title	Sample Type	Desc
APS ultrasound assisted synthesis 1.0	Nanoparticle	Prep only Doc
APS Heat assisted Synthesis 1.0	Nanoparticle	Prep opti Doc
Fluoprobe 565A, Liquid Phase Approach 1.0	Nanoparticle	Fluc App Doc
Fluoprobe 565A, Magnetic Reactor Method 1.0	Nanoparticle	Fluc Doc
APS PEG Functionalization 1.0	Nanoparticle	PEC Doc
PVA quantification 1.0	Nanoparticle	Poly Doc
PCS size and zeta potential measurement (UniFR) 1.0	Nanoparticle	Part Doc
Turbidity measurement 1.0	Nanoparticle	Turt Doc
Cell counting and viability 1.0	Nanoparticle	- Doc

NDR ID	NDR ID on Reception	Title	Type/Status	Info	Action
050007	-	PVA-SPION-MB3-071211	Nanoparticle State: Generated	i	
050018	-	PVA-SPION-MB3-071211	Nanoparticle State: Submitted sent to: CSEM	i	sent on: 2012-01-18
050019	-	PVA-SPION-MB3-071211	Nanoparticle State: Submitted sent to: Estapor	i	sent on: 2012-01-27
050020	-	PVA-SPION-MB2-180811	Nanoparticle State: Generated	i	
050026	-	PVA-SPION-MB2-180811	Nanoparticle State: Submitted sent to: CSEM	i	sent on: 2011-10-12
050027	-	PVA-SPION-MB1-181110	Nanoparticle State: Generated	i	
050028	-	PVA-SPION-MB1-181110	Nanoparticle State: Submitted sent to: UniGE	i	sent on: 2011-03-17

Combined solution

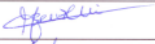



NanoDiaRA
Particles, Molecules & Cells · Diagnosis in-vitro
& in-vivo · Rheumatoid Arthritis & Osteoarthritis



**ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE**

PRUSSIAN BLUE METHOD FOR IRON QUANTIFICATION IN SPION FORMULATION

Function	Name	Date / Signature
Author	Document control	Marie-Gabrielle Beuzelin Olivier 
Approvals	Director LTP	Pr Heinrich Hofmann 

SOP No. SPIONs PR 14-1

Becomes effective on 30.08.2012

Document being replaced -

SUMMARY

This following protocol describes the colorimetric method use for $\gamma\text{Fe}_2\text{O}_3$ SPIONs iron concentration estimation. It is based on reaction between ferric chloride (after dissolution of SPIONs with 6M HCl into Fe^{3+}) and ferrocyanide that lead to the formation of Prussian blue (blue color):

$$\text{Fe}^{3+} \text{ (from dissolved SPION)} + \text{K}_4\text{Fe}^{2+}(\text{CN})_6 + 3 \text{H}_2\text{O} \rightarrow [\text{Fe}^{3+}_4(\text{Fe}^{2+}(\text{CN})_6)_3]$$

The higher is the iron (ferric iron) content the darker will be the staining. The detection limit of this method is 5-10 $\mu\text{g Fe/mL}$.

MATERIALS REQUIRED

INSTRUMENTS

1. Water purification system
2. Incubator 37°C, 5% CO_2
3. Centrifuge
4. Plate shaker (Eppendorf, Thermomixer)
5. Plate reader (Tecan, Infinite 200)

CONSUMABLES

Consult latest "List of lab material" spreadsheet for current or alternative suppliers and part numbers.

chemicals

1. Cell line see SOP Cells PR
2. SPIONs suspension see SOP SPIONs PR 1.1 SPIONs Synthesis
3. Hydrochloric acid (HCl) 37% for analysis (CAS 7647-01-0)
4. Nitric acid (HNO_3) 65% for analysis (CAS 7697-37-2)
5. Chlorure de Fer III Hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$), 90-102% (CAS 10025-77-1)
6. $\text{K}_4\text{Fe}(\text{CN})_6 \cdot 3\text{H}_2\text{O}$, 98.5-102% (CAS 14459-95-1)
7. DI water
8. DPBS 1X (GIBCO, cat 14190)

SOP No: SPIONs PR 14-1

Confidential

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ESB - Electronic Sample Book

[Home](#) | [Show property processes](#)

NDR Sample Tracking: Show all processes

Title	Sample Type	Description	Author
Iron Quantification in SPION by Prussian Blue	Nanoparticle	Iron quantification of a SPION suspension by the Prussian Blue Method Documents: SPIONs_PR_14-1_Prussian_blue_method_for_iron_quantification_in_SPION_formulation.pdf	EPFL

Strategies to meet the challenges

- Establishing SOPs following a clear composition
- Establishing rules for document filing
- Using electronic solutions for structured storage and exchange of results and protocols
- We hope this will increase the scientific value of the results of NanoDiaRA, and that they can serve as a standard for upcoming projects.

Acknowledgments

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- Thank you to Margarethe Hofmann-Antenbrink (MatSearch Consulting), Heinrich Hofmann (EPFL) and Francois Roubert (University of Westminster) for the valuable input and support.

Thank you for your attention.