Notification of the end of a clinical trial (ClinO) or of a research project (HRO) to the Ethics Committee

The end of a study (clinical trial or research project) has to be submitted to the (Lead-) Ethics Committee that approved the clinical trial or the research project within **90 days** of its conclusion (ClinO Art 38; HRO Art 22, 36, 40, 43).

The study end report is submitted electronically through BASEC on screen 6 (Lead EC: General and main site's documents) and category 39. Miscellaneous / Varia.

Definition of study end:

The end of a study involving persons in Switzerland is defined as the date of the 'last person (or "patient") / last visit in Switzerland'.

The end of a study not involving persons in the absence of informed consent in accordance with Art. 34 HRA is defined as the date of 'the completion of the collection process'. The period of data collection should be defined in the research project protocol.

Study discontinuation or early termination:

The (Lead-) Ethics Committee must be notified within **15 days** of a discontinuation or early termination of the **clinical trial** (ClinO Art 38, Abs. 2). In a multicenter clinical trial the Lead Ethics Committee will inform the concerned ECs.

The (Lead-) Ethics Committee must be notified within **90 days** of the discontinuation or the **research project** (HRO Art 22, 36, 40).

Final clinical trial report:

A final clinical trial report should be submitted to the (Lead-) Ethics Committee within **a year** after completion or discontinuation of the **clinical trial**, unless a longer period is specified in the protocol (ClinO Art 38, Abs 3).

In multinational clinical trials, the final report should be submitted within a year after the global completion or discontinuation of the multinational clinical trial.

The final report is submitted via BASEC on screen 6 (Lead EC: general and main site's documents) and category 41. Final report.

This notification concerns the end of a Clinical Trial (Clinical Trials Ordinance, ClinO) or the end of a Research Project involving persons (Human Research Ordinance, HRO Chapter 2)	Yes ☒ No ☐ **If Yes, complete sections 1 - 8**
This notification concerns the end of further use of health-related personal data and/or biological material for research, research involving deceased persons or research involving Embryos and Fetuses from induced abortion and from spontaneous abortions including stillbirths (Human Research Ordinance, HRO, Chapters 3, 4, 5)	Yes ☐ No ☒ **If Yes, complete sections 1 - 3, 8**

1. General study information

BASEC or PB_BASEC ID number	2021-00099
Title of the study	Crying, unsettled and distressed infants: Swiss arm of an international randomised controlled trial to test the effectiveness of osteopathic care
Lead Ethics Committee (Swiss EC only) - For multicentric study with a Lead EC, or for monocentric research project. - If the study has neither a BASEC nor a PB_BASEC ID number, indicate here the Lead EC reference number.	CER-VD
Participating Ethics Committee (Swiss EC only) - For multicentric study only. - If the study has neither a BASEC nor a PB_BASEC ID number, indicate here the participating ECs reference numbers.	CER-GE
Sponsor	Main Sponsor: Steven Vogel, University College of Osteopathy Swiss Sponsor: Nataly Viens Python, HES-SO
Applicant - If different from the sponsor.	Dr. Paul Vaucher

Was the study carried out in other countries than Switzerland?	Yes ☒ No ☐ (Swiss study only)

2. Early termination

Has the study been terminated prematurely?	No ☒ go to section 3. Study duration Yes ☐ globally If yes, give the date of the early termination: [day/month/year] Yes ☐ in Switzerland only If yes, give the date of the early termination in Switzerland: [day/month/year]

3. Study duration

Date: Study start in Switzerland - Study involving persons: Date first patient/ first visit in Switzerland. - Study not involving people: data/sample collection started.	25/09/2021
Date: End of study in Switzerland - Study involving persons: Date last patient / last visit in Switzerland. - Study not involving persons: data/sample collection completed.	28/06/2022
Study completed globally?	Yes ☒ No ☐ N/A ☐ (Swiss study only)

4. Details on participating center(s)

Number of participating center(s) in Switzerland	
Open center(s): 5	Active center(s): (center(s) that enrolled at least 1 participant) 2

Twenty-four osteopaths expressed interest for contributing to the trial. Fourteen of them followed the training. Nine osteopaths returned their signed agreement form for participating. However, four of them were practicing in other cantons than those for which ethical approbation was obtained and could not contribute.

5. Details on recruitment

<table>
<tr><th colspan="4">Number of participants in Switzerland</th></tr>
<tr><td>Target number:
40</td><td>Enrolled:
4</td><td>Prematurely terminated (drop-outs):
4</td><td>Completed:
4</td></tr>
<tr><td colspan="2">If possible, explain any gap between target number and enrolled number of participants</td><td colspan="2">Due to unplanned obstacles, recruitment objectives were not met during the trial. These obstacles were:

• Recruitment limitations due to covid-19 restrictions.
• Three months delay in starting the trial as the sponsor only noticed it was not insured for RCTs after ethical approbation was sought. Initially, the institution had provided written confirmation that the study was covered by the overall liability insurance for the State of Fribourg.
• Difficulties in obtaining ethical approbations for running the study in the German and Italian speaking parts of Switzerland. The ethical committees required all participating osteopaths to be identified and trained prior to approbation. This was impossible to organize as the trial did not have the human resources ta have all osteopaths trained at once and to assure quality control in a short period of time. It was initially planned to recruit osteopaths progressively. This was refused by the Bern, Zurich and Ticino ethical committees making it impossible to start the study with the osteopaths that were already trained. Furthermore, the study budget for ethical approbation had planned 1500.-. The additional 800.- requested by other ethical committees was unexpected. Financial sources were not available to obtain ethical approbation separately from each CE from SwissEthics. We had little other choice than to drop all recruitment opportunities from most of Switzerland.

Measures were taken to increase recruitment opportunities:

• The trial was extended for 9 months.
• The Fribourg Hospital was included as a partner for recruitment. However, given the service in which the study was to take place had never directly contributed to a RCT, personnel had to be trained and internal obstacles made it impossible to set up the study in time for them to contribute.
• Specific interviews and investigations were planned individually with each contributing osteopath to understand barriers and improve recruitment. The main barriers were:
  • Difficulties in having patients accept randomisation for an intervention that is already delivered and they believe to be beneficial.</td></tr>
</table>

	• Rome IV criteria for "colic" is based on overall crying time whereas parents seem to visit osteopaths based on changes in behaviour and infants attitudes. Most infants consult with lower crying times than those required by the protocol and could not be included. The Data Monitoring Committee used the pilot data to measure more precisely the required sample size. Modification in the statistical plan accounting for multiple measures showed that the trial could reach the planned power with a smaller sample. It was decided to continue the trial. The final analysis reached the set power even if only 66 participants were included.

6. Participants' safety

Number of safety cases of participants included in Switzerland			
Fatal cases: 0	Serious Adverse Events (SAEs): 0	Serious Adverse Drug Reactions SADRs (only for IMPs) n/a	Suspected Unexpected Serious Adverse Reactions, SUSARs (only for IMPs) n/a
Have all safety cases been reported to the (Lead-) Ethics Committee within the regulatory timelines?		Yes ☒ No ☐ N/A ☐	
If no, explain the reason - submit any outstanding safety reports, as applicable.		As a side note, two severe adverse events were observed with hospitalization in the UK. These were reported to the Sponsor in accordance to good clinical practice and UK regulations. None of the two cases were deemed in relation to the trial or patient management by the osteopaths.	

7. Final study report (clinical trials only)

Is a summary of the final report on the clinical trial available and enclosed with this form?	Yes ☐ No ☒ If No, submit to the (Lead-) Ethics Committee within a year after completion or discontinuation of the clinical trial.

8. Signature of the applicant

I hereby confirm that / confirm on behalf of the sponsor that (cross out what is not applicable):

- The above information given on this declaration is correct; and

- for ClinO study only, that the clinical trial summary report will be submitted to the (Lead-) Ethics Committee within a year after completion or discontinuation of the clinical trial, unless a longer period is specified in the protocol.

Date and place: Fribourg, 14/09/2022

Print name: Paul Vaucher

Signature: