TERMS OF REFERENCE: Incidental Findings (IFs) - Informed consent specifications and communication process in Luxembourg

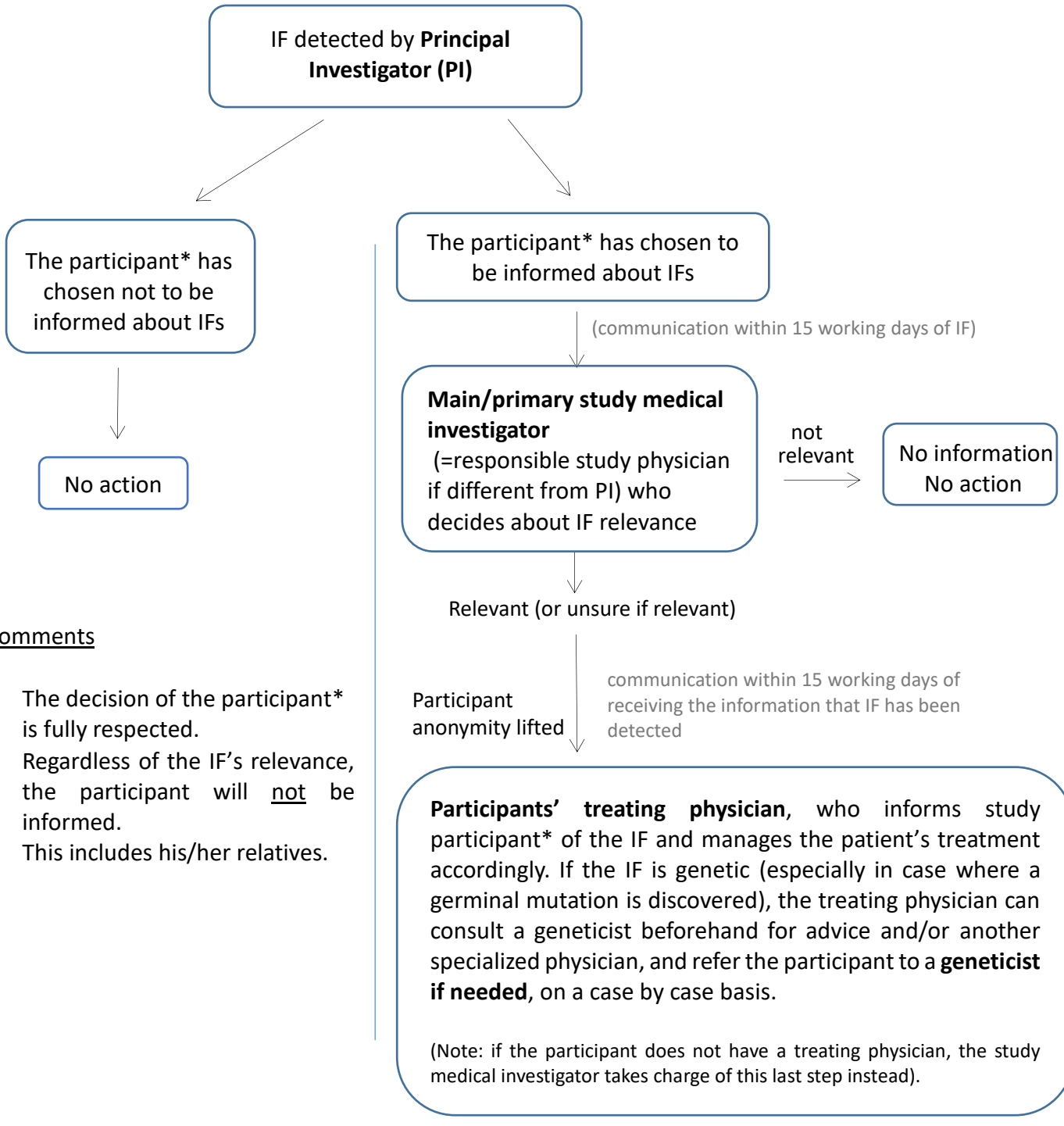
Version dated 12.10.2022

Note: this document might be updated in the light of more experience.

Process

The scope of this procedure is in relation with Incidental Findings (IFs) in the frame of research studies

An IF is defined as: *"Information that may be of potential health or reproductive importance that are beyond the aims of the study"*.



Comments

- The decision of the participant* is fully respected.
- Regardless of the IF's relevance, the participant will not be informed.
  This includes his/her relatives.

* or his/her legal tutor in case of incapacity of the participant consent

Remarks

- Participant is defined as the person (donor, healthy or not) who participates in the study. If the participant is incapable of giving consent his/her legal tutor can decide and sign the informed consent form on his/her behalf.
- There is agreement, by definition, because incidental findings are really incidental, that there is no obligation to actively search for genetic mutations or other types of potentially health-relevant "findings".
- Time window in which IFs may occur and would then be communicated to the responsible study physician (if different than PI) and then to treating physician: at time of analysis. In practice, the researcher has 15 days to communicate the IF to the responsible study physician. The latter then has 15 days to decide whether the IF is relevant and, if the answer is yes, to communicate it to the treating physician in case he/she thinks the IF is relevant (or is unsure); this implies that the study physician lift the study participant's anonymity to be able to contact the treating physician. Note: this new version of the terms of reference applies also to secondary uses of samples collected in the frame of a "primary" study. By "study physician", we are referring to the study physician of the primary study (it is thus implied that a study physician should always be involved in the primary study).
- The participant information sheet and the informed consent form need to clearly reflect the different participants' options.
- The participant should have the possibility to change his/her choice.
- Geneticist: his/her main task is to advise the participant sent to him/her by the treating physician. The geneticist can also advise the treating physician in case the latter does not know how to deal with the information about the IF that he/she has received from the responsible study physician, before deciding whether to refer the patient to a geneticist. The geneticist may be involved in re-contacting the patient directly as well, if deemed best by both the treating physician and the geneticist.

Participant information content in relation to IFs

Below is a high level recommendation; individual adjustments will depend on the research field and specific project.

Principle

The patient information sheet must clearly inform the participant about the different options he has in relation to IFs. The information given to participants regarding IFs must be included in the study participant information sheet.

In the case of whole genome sequencing (WGS), the additional information should be given:

- information on what is genetic sequencing and what are potential incidental findings in that context (including definition)
- Indication that such a finding is not a diagnostic
- Indication that there is no obligation for the researcher to actively search for genetic mutations
- Information on the different participants' options regarding IFs and about the potential consequences of deciding to be informed or not. A separate declaration has to be signed.

→ *Options available:*

- If study participant has decided that he/she does not want to be re-contacted at all --> he/she will receive no information
- If study participant has decided that he/she wants to be re-contacted in case of an IF --> he/she will be informed of the IF with clear information on what such a finding means, through his/her treating physician or a geneticist if the treating physician is unable to manage the IF or decides that the geneticist should contact the patient directly. In the informed consent form, the patient responds *yes* or *no* to the following statement: “I accept that IFs be communicated to me through my treating physician / the responsible study physician / a geneticist if appropriate."

- Information that if an IF occurs, it will be at the time of data analysis (which could be several years after inclusion in the study) within the present study (or further studies if he/she has consented to secondary uses of his/her samples). And that, if he/she decides to be re-contacted in case of an IF, this will also happen only at that time.