SUPPLEMENTAL APPENDICES

APPENDIX S1: Information leaflet reproductive options

Leaflet in English, translated from the original leaflet in Dutch.

Thank you for your interest in the study 'The desire to have children with hereditary skin conditions'! An interview with you is scheduled shortly to discuss your experiences.

The aim of the interview is to gain insight into the thoughts, feelings and/or needs of study participants with a hereditary skin condition who currently want to have children (or wanted to in the past) regarding considering the options for having children.

This leaflet contains information about these options for having children. This will give all study participants a basic understanding of the various options that we can discuss during the interview. Below is a list of the various options for having children.

- Adoption
- Prenatal diagnosis (PND)
- Preimplantation genetic testing (PGT)
- Use of donor gametes
- Refrain from having children
- A natural pregnancy without genetic testing
- Foster care

Each option is explained in detail.

- **Adoption**

Adoption is the legal process of taking in a child who is not biologically related to the adoptive parents.

- **Prenatal diagnosis (PND)**

Prenatal diagnostics is additional testing during pregnancy and involves testing relatively early in the pregnancy (around 11-16 weeks) to determine whether the unborn child has a familial hereditary disorder. This is usually done via a chorionic villus sampling or amniocentesis. A sample of tissue from the placenta or amniotic fluid is taken through the abdominal wall or vagina and examined. This tissue contains the child's genetic material. If the child is found to have the hereditary condition, parents can choose during pregnancy whether to terminate the pregnancy.
- Chorionic villus sampling (11th-12th week of pregnancy): There is a 0.2% risk of miscarriage because of chorionic villus sampling. This risk is in addition to the spontaneous miscarriage risk of 2% around this time.
- Amniocentesis (16th week of pregnancy): There is a 0.2% risk of miscarriage because of amniocentesis. This risk is in addition to the spontaneous miscarriage risk of 0.5% around this stage.
The results of the chorionic villus sampling or amniocentesis are available approximately 3 weeks after the test has been performed. By then, the pregnant woman is well into her second trimester.

• Preimplantation genetic testing (PGT)

PGT, also known as embryo selection, is a method that can prevent the birth of children with serious hereditary disorders. PGT requires in vitro fertilization (IVF) treatment. This means that the woman's eggs and the man's sperm are collected and brought together outside the body (in the laboratory) to allow fertilization to take place. Before this can happen, the woman's eggs must first be brought to maturity using medication to stimulate egg production. An ultrasound scan is used to check whether there are enough follicles, followed by egg retrieval. Egg retrieval involves removing the eggs from

the ovaries so that they can be fertilized with sperm. A fertilized egg is called an embryo. One or more cells are taken from each embryo, and the genetic material of these cells is then examined. The embryos are then examined to see whether they have the hereditary condition. Only embryos without the condition are transferred back into the uterus. This procedure is 95-98% reliable in ensuring that the future child will not have the condition. In other words, the risk of a child being born with the condition for which embryo selection was requested after PGT treatment is small, at 2 to 5 percent.

The success rate for PGT treatment is approximately 20 percent per treatment started. In the Netherlands, three PGT treatments are covered by health insurance, provided there are no special circumstances. On average, 40 to 50 percent of couples achieve an ongoing pregnancy within three treatments.

The duration of the PGT process (from referral to start of treatment) varies greatly and depends largely on the indication. Some couples can start within a few months, while others have to wait a long time, sometimes up to two years. Couples are informed during the intake about the approximate preparation time for them.

The risk of PGT treatment for the woman is the same as the risk of IVF treatment. The risk of complications with IVF is a few percent. One of the most common complications (in 1 to 2 percent of all cases) is overstimulation. This means that too many follicles in the ovaries mature. The woman may then experience abdominal pain and fluid retention. In some cases, the treatment will have to be stopped, and hospitalization may be necessary. Other possible complications include bleeding or infection.

Removing one or more cells from a 3- to 5-day-old embryo does not, as far as is known, harm the embryo's chances of development. Nor has any increase in the percentage of children with congenital abnormalities after PGT been reported in international scientific literature.

- **The use of donor gametes**

The use of donor gametes means that in fertility treatments, such as IVF, sperm or eggs from a donor are used instead of those from the intended parents. This allows a couple who are having difficulty conceiving naturally to become parents with the help of genetic material from a donor.

- **Deciding not to have children**

- **A natural pregnancy without genetic testing**

- **Foster care**

Foster care is a form of care in which children who cannot live with their biological parents are temporarily placed in another family. This family, also known as a foster family, provides the child with a safe and supportive environment.

If you have any questions or concerns, you will have the opportunity to discuss them with the researchers at the beginning of the interview.

APPENDIX S2: Pre-interview questionnaire

Questionnaire in English, translated from the original questionnaire in Dutch

1. What is your name? _____
2. What is your date of birth? _____

3. What is your age? _____ years

4. What is your nationality? _____
5. What is your gender? ☐ male ☐ female
   ☐ other ☐ I prefer not to say

6. What is your marital status? ☐ unmarried ☐ married
   ☐ living alone ☐ co-habiting
   ☐ widowed ☐ divorced
   ☐ single ☐ registered partnership
   ☐ other

7. How long have you been with your current partner? _____

8. What is your highest completed level of education?
   ☐ none
   ☐ primary education
   ☐ lower vocational education
   ☐ secondary vocational education
   ☐ bachelor's degree university/applied sciences
   ☐ master's degree university/applied sciences
   ☐ PhD of post-doc
   ☐ Other, namely:

9. What is your employment status? ☐ employed, fulltime
   ☐ employed, parttime
   ☐ unemployed, seeking employment
   ☐ unemployed, not seeking employment
   ☐ unable to work
   ☐ retired
   ☐ Other, namely:

10. What is your profession or position? Most recent? _____

11. Do you consider yourself to belong to a religious or philosophical group?
    ☐ Christianity, Roman Catholic

☐ Christianity, Protestant
☐ Judaism
☐ Islam
☐ Hinduism
☐ Buddhism
☐ Other, namely:
☐ I do not belong to any religious group

12. Do you have a hereditary skin condition yourself, or are you a carrier of a hereditary skin condition?

☐ I have a hereditary skin condition
☐ I am a carrier of a hereditary skin condition
☐ Other, namely:

13. Which hereditary skin condition has been diagnosed in you? _____

14. Have you undergone genetic testing for your hereditary skin condition?
☐ yes ☐ no ☐ unknown

15. If so, what mutation/pathogenic variant was found? _____

16. When did you first experience skin symptoms consistent with your hereditary skin condition?
☐ From birth/preschool (0-4 years)
☐ Primary school period (4-12 years)
☐ Teenage period (12-18 years)
☐ Adulthood (>18 years)
☐ No symptoms carrier status

17. Are you being treated by a dermatologist for your hereditary skin condition?
☐ Yes, I visit the dermatologist for a check-up at least once or twice a year
☐ Yes, I visit the dermatologist for a check-up every few years
☐ I used to be monitored by a dermatologist, but not anymore
☐ No, I have never been under the care of a dermatologist
☐ Other, namely:

18. Are you currently taking medication or receiving treatment for your skin condition? ☐ yes
☐ no

19. If so, what medication are you currently taking or what treatment are you currently undergoing for your skin condition? _____

20. What symptoms or complaints are you currently experiencing from your hereditary skin condition?
☐ Itch
☐ Desquamation
☐ Hyperkeratosis
☐ Dry skin

☐ Pain or burning sensation
☐ Cosmetic disturbance
☐ Blisters, pustules or wounds
☐ Alopecia
☐ Teeth or nail complaints
☐ Inability to sweat
☐ History of skin cancer
☐ Other, namely:

21. On a scale 1-10, how much impact does your skin condition have on your daily life? 0 = no impact en 10 = significant impact + explanation _____

If you are a carrier of a hereditary skin condition:
22. You have indicated that you are a carrier of a skin condition. A carrier is someone who carries a genetic disease or abnormality, but usually has no symptoms themselves. Do you have symptoms or complaints that are consistent with the hereditary skin condition?
☐ yes ☐ no ☐ other, namely:

23. Does anyone in your family have the hereditary skin condition that you are a carrier of?
☐ yes ☐ no explanation _____

24. Do you currently have a desire to have children? Or did you have this in the past?
☐ Yes, I/we currently desire to have children, but do not yet have any children.
☐ Yes, I/we had a desire to have children in the past and have had a child/children.
☐ Yes, I/we had a desire to have children in the past, but ultimately decided not to have (biological) children.
☐ No, I/we never had a desire to have children.
☐ No, I/we do not have an active desire to have children but may want children in the future.
☐ Other, namely:

25. Do you have children? ☐ yes ☐ no

26. If so, how many children do you have? _____

27. Which of the following options applies to your situation?
☐ Yes, I/we have biological children
☐ Yes, I/we have biological children through prenatal diagnostics or pre-implantation genetic testing
☐ Yes, I/we have used donor gametes
☐ Yes, I/we have used adoption
☐ Yes, I/we have children through foster care
☐ Other, namely:

28. Do your children have the hereditary condition that you are affected by? _____
29. Do you have experience with reproductive counselling? If so, please explain. _____

APPENDIX S3

Data analysis, qualitative background of research group and reflexivity

Data analysis process

Each line of interview data was assigned an initial code, often using the participants' own words, by reading it in the context of the research question. F.v.V and O.B. independently coded the first five transcripts, comparing on each other's codes and themes to reach consensus in case of differing interpretations and, after discussion, a final agreed-upon code was formulated. Due to high coding similarity between F.v.V and O.B., the remaining transcripts were initially coded by F.v.V. and reviewed by O.B. Clustering into representable themes and subthemes was done together with the research team. No themes were created in advance but derived from the interview data. Furthermore, field notes were made during and/or after the interviews, which were used for the summaries of the transcripts (principle of member checking).

Qualitative background of research group and reflexivity

F.v.V. is a PhD student in dermatology and clinical genetics, with medical and research qualifications (female, MD, MSc and BSc). She previously published qualitative research involving interviews and thematic analysis and attended qualitative methodology courses. O.B. is a dermatology medical student with a research degree (female, BSc). P.S. is an academic and clinical professor of dermatology with expertise in genodermatoses. L.v.O. is a clinical psychologist and an experienced qualitative researcher who previously published original qualitative research. K.V. is a patient representative from the Dutch and European patient association of ichthyosis and provided input from a patient perspective. F.T. is a clinical geneticist with expertise in genodermatology and J.C. is a dermatologist with expertise in genodermatology. M.v.G. is a laboratory specialist with expertise in genodermatology. K.M. is an academic and clinical professor of dermatology with expertise in BCNS/Gorlin syndrome. M.H. is a clinical geneticist with expertise in PGT. A.G. is a dermatologist with expertise in genodermatology and previously published qualitative research involving interviews and thematic analysis. This research group included senior qualitative experts and experts in the field of genodermatology and PGT. None of the participants had clinical interactions with the interviewers. At the start of each interview, the researchers (F. v. V. and O. B.) introduced themselves to the interviewees and explained the purpose of the study.