Chapter 8: Ethical Review in Life Sciences Research

Abstract: As was noted in week 6, Engineers do not simply make up their own mind as to whether their behaviour is ethical: rather they normally have to justify their decisions, and this includes doing so before their peers in some way. Where research involves humans or animals there is a formal – often legal – process for this.

- In Switzerland animal research is governed under the *Ordonnance sur la protection des animaux* (OPAn, 2008). In the canton in which EPFL is based, this means proposals to carry out research on animals are reviewed by the *commissions cantonales sur l'expérimentation animale*.
- For research with humans which concerns human diseases or the structure and function of the human body, this is governed by the *loi relative à la recherche sur l'être humain* (LRH, 2011); proposals to carry out this kind of research are reviewed by the *Commission cantonale d'éthique de la recherche sur l'être humain*.
- For other research with humans, each institution identifies its own ethical procedures. In EPFL all other research involving humans is subject to review by the Human Research Ethics Committee (HREC) which provides both an ethical review and a review of compliance with Swiss Data Protection Law (*Nouvelle loi sur la protection des données*, nLPD, 2023).

Ichthyotherapy treatment for psoriasis

Psoriasis is a skin disease that causes a rash with itchy, scaly patches, most commonly on the knees, elbows, trunk and scalp. Psoriasis is quite common, affecting 2-3% of the population worldwide. It appears more common in Europe than in Asia. It is a long-term (chronic) disease with no known cure. It can be painful, and pain and itching can interfere with sleep and can also make it hard to concentrate.

'Ichthyotherapy' (also called 'fish pedicure' or 'fish spa') has emerged as a potential treatment for psoriasis symptoms. Two prior studies (Özçelik et al, 2000; Grassberger et al. 2006) have suggested that it may be effective. In Ichthyotherapy, the hands, feet, and potentially the whole body are immersed in a pool or tub of water filled with the fish *Garra rufa* which feed on dead human skin. The same process is also widely used for cosmetic purposes to reduce hardened skin/calluses. The *Garra rufa* fish in their natural habitat eat plankton, but, in a hot

spring environment in Turkey in which plankton was scarce, it was noted that the hungry fish ate dead human skin. This led to the development of the cosmetic and potential therapeutic treatment.

Your team plan to study the effectiveness of 'Ichthyotherapy' against psoriasis. This can be considered as a Phase II trial (since fish pedicures are already widely used for cosmetic purposes you assume that it is not necessary to carry out a Phase I test of safety with a small group of volunteers).

Based on a review of the prior studies, your initial plan is to recruit 100 people with moderate to severe psoriasis (Psoriasis Area and Severity Index [PSAI] scores higher than 8). These will be treated for 2 hours per day, with a full body bath in a fish tank. You plan to have 5 tanks that can each take 5 people at a time, (5 people per tank X 5 tanks X 4 sessions per day). The treatment will be followed for 14 days. Effectiveness will be measured using the Psoriasis Area Severity Index (PASI) score after 14 days of treatment, and 7, 14 and 28 days after treatment. As the effectiveness of standard treatments is known, it is not necessary to have a control group: standard treatments (steroidal cream) give rise to on average a 75% reduction in PASI score, so a 'successful' outcome is measured as having a reduction in PASI score >75%.

1. What are the people or entities who are involved in this social network?
2. Let's focus on (a) the fish, (b) the psoriasis patients in the study, (c) the researchers, (d) those involved in caring for the fish, (e) the wider scientific community. For each of these, identify their perspective on this study.

3. For the groups (b) to (e), identify what emotions you think they might experience in relation to the study. For the fist, identify what sensations you think they might experience in the study.
4. Are there particular technical competences that are relevant that you expect a life sciences researcher to display in a situation like this? Are there particular principles or practices described in a relevant code of ethics that might be applied here?
5. Without studying the question in detail (i.e. based on your prior knowledge), do you foresee any problems with your initial plan which makes you think it might need to be modified (you should not consider this your final answer to this question – we will come back to it below)?

Introduction

In chapter 6 we saw that part of the process of applying ethical principles to a situation was the process of *justification*. This involves reviewing any ethical proposition against several criteria to see if it makes sense:

- Are there *reasons* for an action that can be stated clearly?
- If there is a reference to *evidence* or facts of a situation, is the evidence based on good empirical research?
- Are these reasons *consistent* or do they contain internal contractions?
- Are the conclusions *intuitively plausibility*?
- Are all the important facets of the situation taken into account (*comprehensiveness*)?
- Is the argument as *simple* as is reasonably possible?

Justification does not simply mean justifying the action to yourself (although that is, of course, seen as important in the deontological perspective). It also means being able to explain your justification to others. This principle has been identified in bioethics from the early post second world war period. For example, the Helsinki Declaration (1964) is one of the early professional ethics codes for medical researchers. It states that a research project

"must be submitted for consideration, comment, guidance, and approval to the concerned research ethics committee before the research begins". This principle of public justification is also still found in more recent and specific codes: the EPFL Lex 3.3.2, for example, states that research involving animals must be "justifiable before the authorising bodies, ethical committees, animal welfare officers and the general public" (Article 9, para 2). This idea of needing to validate your ethical proposition with other people is one that is now core to ethics processes in most organisations and at national levels.

Reflection question

Think back to the case study at the start of chapter 6 'Testing Heat Treatment for Infected Blood Products'. How might a requirement for external review by peers have impacted on the design of Peter Kernoff's study (which involved treating "previously untreated patients", (PUPs) with potentially infected blood products)?

We noted in chapter 7 that, at a national level, ethical principles are often written into national laws which operate as a kind of enforced ethical code. In Switzerland, there are at least three different laws which are potentially relevant to research in life sciences.

- In Switzerland animal research is governed under the *Ordonnance sur la protection des animaux* (OPAn, 2008).
- For research with humans which concerns human diseases or the structure and function of the human body, this is governed by the *loi relative à la recherche sur l'être humain* (LRH, 2011).
- Any research project which involves the collection of data from identifiable people is subject to Swiss Data Protection Law (*Nouvelle loi sur la protection des données*, nLPD, 2023).

All three of these laws require that the researcher does not simply decide by themselves whether or not their research is ethical and appropriate, but rather that the research proposal is reviewed by some independent experts who can validate its compliance. This is called peer review.

Ordonnance sur la protection des animaux (2008)

Switzerland is generally regarded as having a high standard in animal welfare legislation. In Switzerland vertebrate animals are legally identified as having an inherent dignity which needs to be respected. This means that any use of an animal that inflicts pain, suffering, harm or anxiety on animals needs to be justified by some greater. This applies not only to animal experimentation but to animal use in other areas (such as domestic animals and farming).

Chapter 6 of the Animal Protection Law deals with animal experimentation. The key ideas are:

- Animal experiments that affect the welfare of animals can only be carried out where they are identified as 'indispensable', This means that the aim of the experiment cannot be achieved by methods which do not require animal experiments.
- An animal experiment must be planned so that the smallest number of animals necessary is used and the least possible stress is inflicted on the animals. The 3R principles are applied: animal experiments must be *replaced* with other types of study where possible, the number of animals used should be *reduced* to the minimum (in line with statistical knowledge), and methods should be *refined* to reduce the pain and distress on animals, where possible.
- A severity analysis and harm-benefit analysis is required in which the gain in knowledge is weighed with respect to the distress to animals.
- Animals intended for experiments must come from an authorized Swiss animal facility or from a foreign facility that is accredited by the Swiss authorities. Captured wild animals can only be used if sufficient numbers cannot be bred.

- Experimental animals must be treated with care. Their welfare must be monitored throughout the experiment so that pain, aches, damage and anxiety, as well as disturbances in general condition, can be recognized. Animals experiencing notable pain should be anesthetised, where the experiment permits.
- Stopping conditions for an experiment must be defined in advance.

Severity of distress to animals in Switzerland is measured on a 4 point scale:

- 0: No constraint placed on the animal (typically observational studies)
- 1: Slight constraint (short term pain suh as through taking repeated blood samples over 24 hours)
- 2: moderate constraint (pain that necessitates anaesthesia, such as surgical procedures with some post-operative pain)
- 3: severe constraint (severe or continuous pain, significant fear or impairment)

A harm-benefit analysis is required in proposals for animal research. Level 3 distress is typically only justified in research on serious and complex diseases such as cancer, epilepsy, Alzheimer's disease, multiple sclerosis and other autoimmune diseases as well as organ transplantations and infectious diseases. It is normally only justifiable where previous research indicates that there are expected benefits which suggest that the study benefits are high enough.

An application to carry out an animal experiment is reviewed by a canton committee: *commissions cantonales sur l'expérimentation animale*. The process is:

- Write an application which is submitted to the institution and approved by the animal welfare officer (arrow 1, on the figure 1)
- This is sent to the Cantonal Veterinary office (2). The applicant will respond to questions from the cantonal veterinarian
- This is sent to the canton commission for review (3). The applicant will respond to questions form the Canton commission (4).
- An authorised application is sent to Federal Veterinary Office and to the applicant (6).
- The applicant has to wait 30 days after authorisation to allow time for appeal before starting experimentation (7).

The application form can be found here: https://inside.epfl.ch/center-of-phenogenomics/wp-content/uploads/2020/09/Form-A-EN-animex-ch-V1.0-2020-08-11_AWU.docx.

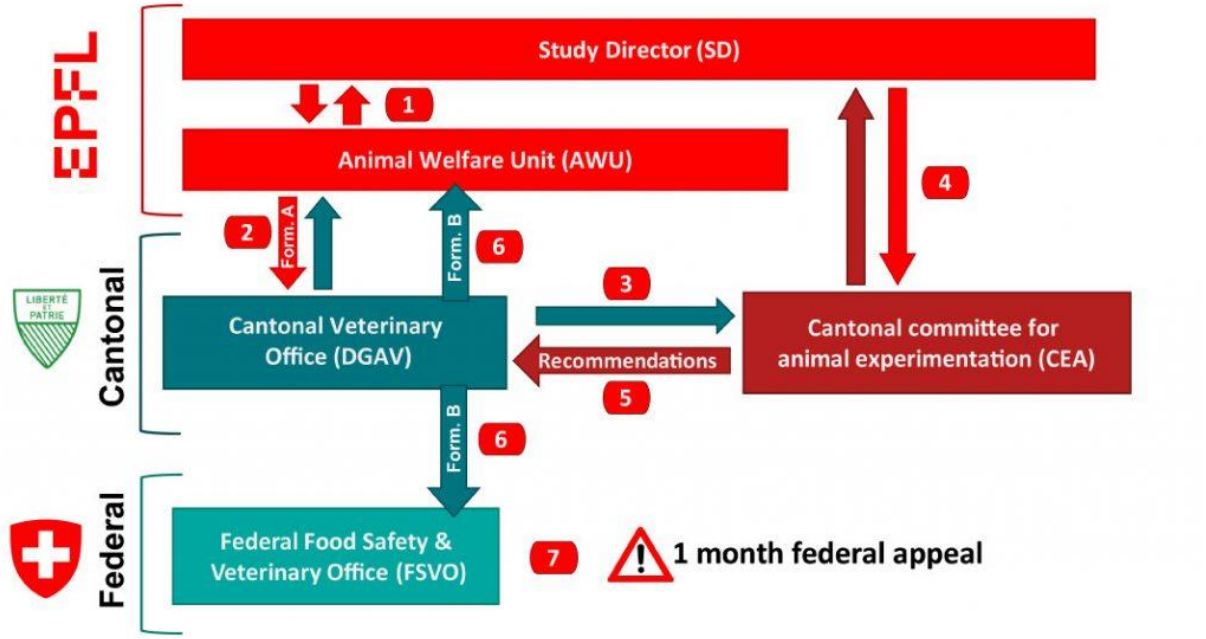

Figure 1: The process of applying for authorisation for animal experimentation

For licencing of medicines and medical products there is also a formal, legal process of review. This is overseen in Switzerland by *swissmedic*.

Questions

The following paper reviews the research and issues with therapeutic fish pedicures:

Shih, T., Khan, S., Shih, S., & Khachemoune, A. (2020). Fish pedicure: review of its current dermatology applications. *Cureus*, *12*(6). https://www.cureus.com/articles/32522-fish-pedicure-review-of-its-current-dermatology-applications.pdf

Identify what it says about animal welfare concerns about the *Garra rufa* fish.

1. How might the 3 R principle be applied in the case of this study?
2. What level of distress do you think the fish may experience in this study?

3. How do you think the research protocol in the psoriasis research project be refined to ensure that the research meets the necessary conditions for animal welfare?

loi relative à la recherche sur l'être humain (2011)

This act regulates research that is carried out concerning human diseases and concerning the structure and function of the human body. This covers medical research but may also cover other kinds of research, such as the use of diagnostic tools or sensors that may have a diagnostic function. The key ideas are:

- The interests, health and welfare of the individual human being shall prevail over the interests of science and society (Article 4)
- Research involving human beings may only be carried out if scientific quality requirements are met, researchers are trained and qualified and international good practice guidelines are met (Article 10).
- Non-discrimination: With regard to the selection of participants in particular, no group of persons shall be disproportionately included in or excluded from research without good reason (article 6)
- A research subject must give their informed consent (article 7). Informed consent requires information about the nature and duration of the intervention, any foreseeable risks, expected benefits for themselves and others, measures to protect their personal data, and their rights. (article 16) Special additional measures are required for research involving children, pregnant women and foetuses, and prisoners. Special conditions are also in place for research in emergency medical situations.

- The persons concerned are entitled to be informed of results relating to their health (article 8)
- In every research project, the risks and burdens for the participants must be minimised as far as possible (Art 12)
- All required safety measures to protect the participants must be put in place by the experimenter (article 15)

Any research covered by the act requires authorisation from a cantonal ethics committee. Ethics committees assess whether research projects comply with the ethical, legal and scientific requirements of this Act. In particular, they shall assess whether the protection of the persons concerned is guaranteed (article 51). Ethics committees must have the professional skills and experience required; it must include experts in various disciplines, in particular medicine, ethics and law; and at least one patient representative (Article 53).

The relevant cantonal committee for EPFL is normally the committee of the Canton of Vaud. The committee has between 30 and 40 members. An application is normally assigned to 7 members for a decision, (fewer can be used in the case of simple applications).

Questions

The following paper reviews the research and issues with therapeutic fish pedicures:

Shih, T., Khan, S., Shih, S., & Khachemoune, A. (2020). Fish pedicure: review of its current dermatology applications. *Cureus*, *12*(6). https://www.cureus.com/articles/32522-fish-pedicure-review-of-its-current-dermatology-applications.pdf

Identify what is says about any human welfare concerns about fish pedicures or fish spas. Drawing on what you find out, how should the research protocol in the psoriasis research project be refined to ensure that the research meets the necessary conditions for human research for medical purposes?

3. If there is any lack of clarity as to whether research is concerned with "human diseases and …the structure and function of the human body", a person can ask first for clarification from the cantonal committee. If the research is of this type then, approval of the canton committee is required. Do *you* think that this research project is subject to the requirements of this law? Why?/Why not?

Nouvelle loi sur la protection des données (2023)

Even if a research project is not covered by a the law on human (medical) research, there remain legal requirements related to the protection of people's data. Wherever personal data is collected from an *identified* or *identifiable* person, this law applies. The specification of 'identifiable' here is important: it means that the law does not only apply if you collect identifying information like a name or ID number. If you collect sufficient different points of information about a person to allow the person be identified then the law applies. This might happen in a survey in EPFL if, for example, you collected data about a person's gender, their age, and their country of origin: if there is only one or a small number of people who share the same characteristics then they are *identifiable* (even if they are not identified). So in this case, the law would apply.

The law includes a number of provisions:

- Sensitive personal data can only be processed with a person's consent

- Adequate data security measures must be in place
- Data can only used for the purposes for which it is collected, and it must be anonymized or destroyed as soon as possible
- Where data may be matched with other data and used for generating a profile of someone's personality this is regarded as a high risk activity and is subject to additional constraints. This applies particularly to the use of new technologies in (i) large-scale processing of sensitive data (machine learning) or (ii) systematic monitoring of public areas.

Sensitive data is defined in the law (article 5) as:

- data relating to religious, philosophical, political or trade union-related views or activities,
- data relating to health, the private sphere or affiliation to a race or ethnicity,
- genetic data,
- biometric data that uniquely identifies a natural person,
- data relating to administrative and criminal proceedings or sanctions,
- data relating to social assistance measures;

Question:

1. Are there things included as sensitive data which surprise you? Are there additional data types that you would have included?
2. How might restrictions on collecting certain data types (principle of privacy) conflict with the principle of justice?

For projects that are not already reviewed by a cantonal committee, institutions (like EPFL) assures that research is carried out in line with this law through a review process.

Apart entirely from the needs of data protection legislation, many research funders (Swiss National Science Foundation; EU Horizon programme) and many journals now also require that a project undergoes ethical review.

In EPFL these two functions (legal data protection review and ethical review) are both carried out by a Human Research Ethics Committee (HREC). The HREC application form can be found here:
https://docs.google.com/document/d/1PbY9oeV1SEIKEjqoSamSwH_cn7C0eEdj/edit?usp=sharing&ouid=102171204036425933301&rtpof=true&sd=true

This must include a Data Management Plan.
https://www.epfl.ch/campus/library/services/services-researchers/rdm-guides-templates/

An information sheet for informed consent can be found here:
https://docs.google.com/document/d/1-86WMxrzEytgLQQWNkpx6HJCTA8_bO3W/edit?usp=sharing&ouid=102171204036425933301&rtpof=true&sd=true

Writing an Application for Ethical Review

1. Identify the data security measures that would be put in place to protect the data of the participants

2. Using the HREC Template (Section C), identify the ethical issues related to humans that may arise in the research and identify how they would be mitigated in the research design. Structure your analysis under the headings of (i) autonomy and informed consent, (ii) beneficence/non-maleficence, and (iii) justice. Refer to relevant laws and ethical codes in your answer.
3. Using the HREC template, write a draft of an informed consent sheet for the psoriasis study which could be included in an application.

Question

1. In what ways might you expect and ethical review to be similar to or different from a legal review with respect to data protection legislation?
2. Do you see any risks in having these two functions carried out by the same committee? Do you see any benefits?

Ethics and the Law

This chapter has focused a lot on the way peer review process is written into law. The core idea is that the ethical review process is part of a process of 'justification', and that this idea has now made its way into laws (which are, in effect, ethical codes which are written at national level).

But, as you saw in chapter 7, there are times when the relevant ethical codes say that a researcher or engineer should go beyond what is legally necessary to do what is ethically right. This, then, raises a question as to the relationship between ethics and law. Kotsios et al. (2025) note that there are strong overlaps and parallels between law and ethics but that writers do also establish some differences:

- Law takes time to be made and so law can lag behind ethics in important respects (prior to the 2023 Data Protection Act in Switzerland the relevant law dated to 1992 and so pre-dated large data processing, and cloud storage, for example).
- Laws – especially those related to companies, may not really be enforced and may not be motivating for people to change their behaviour
- Since laws differ in different countries, large companies can exploit differences (animal products brought from other countries may not have been produced to the same ethical standards as in Switzerland, for example)
- Ethics often starts from first principles, while law generally starts from what is already decided (precedent). Hence the logic and support for their arguments are often different.

All of this suggests that the law and ethics are fundamentally different. At the same time, Kotsios et al. (2025) argue that the law can tell us something about what is broadly agreed as an ethical standard and that this can play a role in helping people clarify their own ethical thinking.

Conclusion

In Chapters 6, 7 and 8 we have looked at the kind of principles and ideas that are generally applied in bioethics. As Chapter 6 noted, these are strongly based in a deontological worldview and focuses on the application of a number of broad principles, namely: autonomy, non-maleficence, beneficence and justice. These principles are normally thought to be applied in a reflective way by locating them within a situation, balancing them, and clarifying a decision through a process of justification. In chapter 7 we saw that we don't always have to start from first principles, but rather these principles often exist in forms which are already

specified for different contexts in the form of ethical codes. These codes often go beyond the four principles alone and can also address issues like conflict of interest, trust, honesty and competence. They can be voluntary and aspirational or they can be enforced. One particularly important category of ethical code is the law. As we have seen in this chapter, the law describes many of the ethical principles and specifies how they are to be understood in a national context. The practice of 'justification' is normally written into these laws, typically in the form of ethical review committees. However, even in such contexts where the law does not require ethical review committees (e.g. non-medical or non-biological research with humans), funders, journals and institutions may still require ethical review.

Being able to adequately justify one's ethical position in front of peers is, therefore, an important competence of the life sciences researcher or engineer.

References

Grassberger, M., & Hoch, W. (2006). Ichthyotherapy as alternative treatment for patients with psoriasis: a pilot study. *Evidence-based Complementary and Alternative Medicine*, *3*(4), 483-488.

Kotsios, A., Lennerfors, T.T., & Laaksoharju, M. (2025) Law in engineering ethics educaiton. In Chance, S., Børsen, T., Martin, D.A., Tormey, R., Lennerfors, T.T., & Bombaerts, G. (Eds) *The Routledge International Handbook of Engineering Ethics Education*. Routledge (230 - 244). https://doi.org/10.4324/9781003464259

Özçelik, S., Polat, H. H., Akyol, M., Yalçin, A. N., Özçelik, D., & Marufihah, M. (2000). Kangal hot spring with fish and psoriais treatment. *The Journal of Dermatology*, *27*(6), 386-390.

Shih, T., Khan, S., Shih, S., & Khachemoune, A. (2020). Fish pedicure: review of its current dermatology applications. *Cureus*, *12*(6). https://www.cureus.com/articles/32522-fish-pedicure-review-of-its-current-dermatology-applications.pdf