# From Real-World Challenges to a Global Code: How the PREPARED Code Was Built

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**Abstract.** The PREPARED Code is a risk-based, values-driven framework that integrates research ethics and research integrity and is designed for a global audience. Developed over two years, this ambitious initiative required a collaborative, multidisciplinary effort led by an international team. The PREPARED team employed a range of methods to develop the code, including literature searches, scoping reviews, empirical studies, targeted consultations, ethical and legal analyses, and public consultation. This chapter explores the processes and methods used to develop the PREPARED Code, highlighting how real-world challenges in research ethics and research integrity during crises were identified, analysed and validated by stakeholders. It describes how these challenges were aligned with universally recognised moral values and grouped as risks, and how the risks were transformed into a clear, focused and jargon-free code of conduct. It also details the final stages of development, which involved iterative refinement of the code from Version 1 to Version 13, through extensive consultation and review.

**Keywords:** Research ethics · research integrity · risk-based · code of conduct

## 1 Introduction

The PREPARED Code was envisioned as an operational ethics and integrity framework to facilitate a swift and effective research response during pandemics while upholding key ethical values. Planned to be applicable across all research disciplines, combining both research ethics and research integrity, values-driven, and suitable for a global audience, it was an ambitious endeavour requiring a collaborative and multifaceted approach.

In September 2022, a dedicated team of 16 partner institutions and 14 specialist advisers from five continents set out to develop the PREPARED Code: A Global Code


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of Conduct for Research during Pandemics. Over the next two years, the team conducted literature searches, scoping reviews, empirical studies, targeted consultations, ethical and legal analyses, and a public consultation, culminating in the completion of the code on 31 December 2024.

The work was guided throughout by a carefully designed rationale (see Chap. 3), much of which had been tested during the development of the TRUST Code (TRUST 2018), an ethics code for equitable research partnerships. In fact, the guiding rationale for the development of the PREPARED Code closely mirrored that used for the TRUST Code (Schroeder et al. 2019), including the bottom-up, risk-based, values-driven and inclusive approach (see Chap. 3). However, while guided by a similar rationale, the methods that were implemented for the development of the PREPARED Code differed from those of the TRUST Code as they needed to be tailored to the pandemic context.

This chapter describes the steps taken and the methods employed by the PREPARED team for the development of the PREPARED Code. We first explain how evidence of real-world research ethics and research integrity challenges was gathered, analysed and validated by stakeholders. We then clarify how the challenges were themed and mapped onto globally understandable moral values. The remainder of the chapter details how the PREPARED Team moved from Version 1 of the PREPARED Code to Version 13 through extensive and inclusive consultations.

## 2 The PREPARED Methods: An Overview

The process of developing the PREPARED Code was shaped by a clear rationale or methodological approach as described in Chap. 3. The methodological approach (risk-based, values-driven, etc.) determined the overall strategy for development, but there were many ways in which the strategy could have been implemented. In other words, there were many different methods or "procedures, tools and techniques" (Schwandt 2001: 158) that could have been used to collect and analyse data to inform the development of the PREPARED Code.

For high-quality research, the selection of appropriate methods and procedures must be tailored to the context in which the activities are taking place (Jansen et al. 2010). Additionally, the methods must be consistent with the overall methodological approach (Wright et al. 2016). Table 1 provides an overview of how the project activities were tailored to reveal the research ethics and research integrity challenges relevant to the pandemic context, while remaining aligned to the guiding rationale for the development of the code.

The implementation activities listed in Table 1 were undertaken in a series of steps that flowed from the identification of research ethics and research integrity challenges during pandemics through to the refinement of the PREPARED Code as shown in Fig. 1.

In the following sections, each of these steps is described further to show how they were undertaken.

**Table 1.** Alignment of the guiding rationale (methodology) with activities undertaken during development of the PREPARED Code

| Guiding methodological factor | Implementation activities |
|---|---|
| The PREPARED Code is built on real-world risks | • Literature reviews on research ethics and research integrity challenges during COVID-19 in nine languages<br>• Scoping reviews on research ethics and research integrity challenges during avian flu and Ebola epidemics in English<br>• Literature-based human rights analysis<br>• Empirical and literature-based studies to reveal general challenges for groups in vulnerable situations<br>• Validation workshops to check the identified challenges |
| The PREPARED Code is values-driven | • Values mapping of the challenges to the four values framework of the TRUST Code<br>• Investigation to identify value gaps, e.g. solidarity? |
| Research ethics and research integrity are integrated in a unified code | • Literature reviews on research ethics and research integrity challenges during COVID-19 in nine languages<br>• Scoping reviews on research ethics and research integrity challenges during avian flu and Ebola epidemics in English<br>• Validation workshops to check the identified challenges |
| A broad and inclusive approach to development was taken | • Empirical and literature-based studies to reveal general challenges for groups in vulnerable situations<br>• Creation and involvement of stakeholder platforms for broad code consultation and validation events<br>• Analysis of pandemic/crisis guidance documents to ascertain whether the risk analysis had possibly overlooked any major challenges |

## 3 Gathering Evidence of Real-World Challenges

Fundamental to both the PREPARED Code and the TRUST Code (TRUST 2018) is that they address all major real-world risks. For the PREPARED Code this meant a focus on pandemics and for the TRUST Code a focus on equitable international research collaborations. First and foremost, those risks had to be identified.

For the TRUST Code, this entailed extensive consultation and searching for real cases of inequitable research collaborations, because such cases were not well represented in

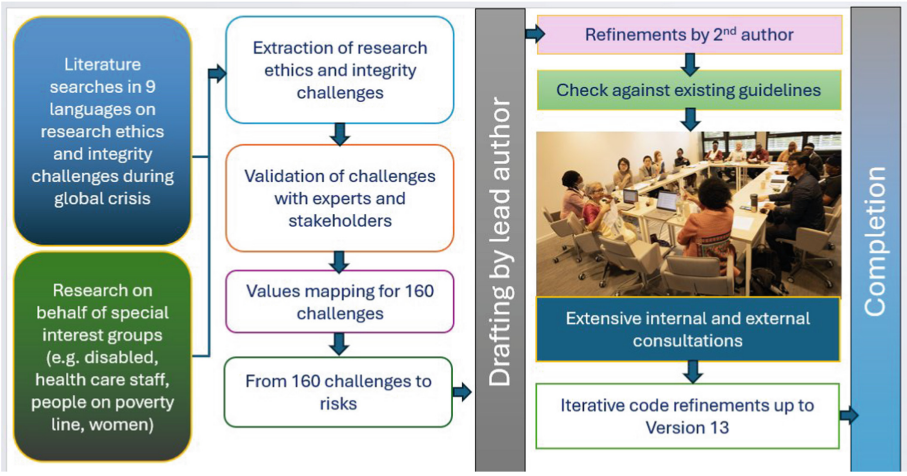


**Fig. 1.** Steps in the development process of the PREPARED Code

the literature. It was even necessary to launch a case study competition to uncover examples of unethical research partnerships (Schroeder et al. 2018).

The situation was very different for the PREPARED Code. COVID-19 saw an explosion in global publishing related to the pandemic (Fassin 2021). The PREPARED team was able to tap directly into this rich body of evidence to identify the research ethics and research integrity challenges encountered during the pandemic. How evidence was gathered is fully described in Chap. 4 and summarised in Table 1 as follows:

- literature reviews on research ethics and integrity challenges during COVID-19 in nine languages
- scoping reviews on research ethics and integrity challenges during avian flu and Ebola epidemics in English
- literature-based human rights analysis
- empirical and literature-based studies to reveal general challenges for groups in vulnerable situations.

The extensive research work spelled out above, undertaken simultaneously in Europe, Africa and Asia, produced a vast amount of rich data for analysis, which began with the extraction and initial sorting of the research ethics and research integrity challenges.

## 4 Extraction of Research Ethics and Research Integrity Challenges

The core analysis team was made up of three people: Hazel Partington and Kate Chatfield (referred to here as the "analysts") and the lead author of the PREPARED Code, Doris Schroeder (referred to here as the "lead author"), who also acted as quality controller throughout.

To ensure that the challenges for research ethics and research integrity were extracted consistently, this was initially done by one person (the lead author), who tabulated the identified challenges in an Excel spreadsheet with one sheet per language.

Following tabulation, the two analysts sorted the challenges into those related directly to research ethics, to research integrity, and to broader "context-specific" challenges that were not specifically related to research (e.g. shortages of personal protective equipment for healthcare staff during a pandemic). Research ethics and research integrity challenges were then inventoried on new Excel spreadsheets that listed each specific real-world research challenge, the reference or source describing it, and which language report it had been identified in.

The resulting tables per language of the original research were checked by the research authors. For example, South Korean colleagues checked that the identified challenges matched those in the Korean language report. Table 2 provides some examples by way of illustration.

**Table 2.** Example of ethics and integrity challenges for research during pandemics

| What happened in the real world? | Reference/source | Which report? |
|---|---|---|
| Interviews and focus groups were switched to digital | Bartmann et al. (2022) | German |
| Outrage erupted at alleged "ethics dumping" after French doctors said that COVID-19 studies should be carried out in Africa, where there was less virus protection | Le Monde with AFP (2020) | French |
| The Sputnik vaccine's efficacy and safety were allegedly announced before clinical trial completion | Cohen (2020) | Russian |
| In a multicentric trial involving 42 sites, the decision of the Central Ethics Committee was followed at only three sites | Bassi et al (2022) | Hindi* |
| Uncoordinated, low-powered studies were conducted in multiple locations | Jung and Kim (2020) | Korean* |
| Healthcare providers had insufficient time to collect the follow-up data on patients necessary for study completion | Liu et al. (2020) | Chinese |
| The use of online platforms with weak security features raised concerns about potential breaches of confidentiality | Ghooi (2020) | English |
| Pre-prints and fast-tracked publications decreased scientific rigour and increased the number of publication retractions | Bermúdez and Maldonado (2021); Dadalto et al. (2020) | Spanish |

* *The Hindi and Korean literature review also included items reported in English about India and South Korea, given that English is an important language of scholarly communication regarding national research ethics matters in those countries.*

Following the sorting and checking, and the removal of context-specific challenges, a total of 160 research ethics and research integrity challenges were identified.

Together, the findings from these reviews provided a detailed and inclusive mapping of global research ethics and research integrity challenges. Since all the challenges were extracted from real-life cases, they offered a representative and nuanced foundation for the development of an ethics code that could be globally relevant while taking special account of groups in vulnerable situations.

## 5 Validation of Challenges by Stakeholders

In the next step of the development process, the experiences and perspectives of stakeholders (including experts) who had faced research ethics and research integrity challenges in practice were explored to confirm that their insights were in line with what had been found in the literature and empirical studies. The PREPARED team also hoped to uncover any additional challenges that had not yet been identified.

To this end, online focus group discussions, called "validation workshops", were convened. These workshops brought together the stakeholders who had experienced research ethics and integrity challenges first-hand, or who could speak with authority on behalf of the groups or networks they represented. Four separate online workshops were conducted with research policymakers, ethics and integrity experts, senior researchers from various disciplines, and representatives from disease-specific European advocacy groups.

Experts were recruited from established networks, including the European & Developing Countries Clinical Trials Partnership (EDCTP), the European Network of Research Ethics Committees (EUREC), the European Network of Research Integrity Offices (ENRIO) and pan-European advocacy groups, aiming for a balance of expertise and diverse perspectives.

Each workshop began with an introduction to the PREPARED project, followed by a presentation of the key research ethics and research integrity challenges that had already been identified. During the discussions, facilitated by Natalie Evans, the stakeholders highlighted challenges specific to their group and how they thought these challenges might be addressed via the PREPARED Code. Some illustrative examples of input per group are given below.

*Policy and research ethics experts* emphasised the need for practical operational guidance for research ethics committees during health crises. They discussed the importance of good communication across decision-making levels and clearer guidance on issues like online consent and multisite trial adjustments. They stressed challenges in returning to normal procedures post-pandemic and the need for additional resources and innovative training. They also highlighted justice considerations, particularly fair benefit-sharing for low- and middle-income countries.

> For the sake of fairness and justice, I think it would be good to demand that researchers address human rights and human dignity because the question usually would be: what is the significance of any study that is being conducted and what are the possible risks and benefits? Researchers trying to deal with this would be looking at it from the lenses of human rights and human dignity so that ethical considerations would be made for individual participants and the public.
>
> Dr Lillian Omutoko, Associate Professor, University of Nairobi and National Bioethics Committee Member

*Research integrity experts* highlighted the fact that the pandemic had exacerbated existing research integrity challenges, but also accelerated the adoption of solutions like open data and living reviews (systematic reviews that are continually updated with new relevant evidence). Transparency issues, data-sharing barriers, a lack of coordination

and collaboration between sectors, and difficulties communicating science to the public were discussed. Improved public communication and transparency about uncertainties were seen as critical for building trust.

> There was such a huge gap between how researchers talk about what they're doing, how it's communicated within science, and how the public at large understands this communication. Or rather doesn't understand it at all and feels that this is all very uncertain and can't be trusted…. Trust in a very important institution, science, was eroded. There's no easy solution to that.
>
> Sabine Chai, Managing Director, Austrian Agency for Research Integrity

*Researchers from diverse disciplines* discussed which knowledge had been prioritised in the pandemic policy response, describing the neglect of attention in pandemic policymaking to some disciplines, such as the social sciences and economics. Researchers also described the negative effects of rushing proposals to chase pandemic funding, and of lockdown measures on the quality of data collection and the training of the next generation of researchers. Like the research integrity experts, they also described the pandemic as exacerbating existing problems within academia and emphasised the need to strengthen research support structures in preparation for the next crisis.

*Expert representatives of European advocacy groups* reported the difficulties their members had in understanding the language used to communicate scientific information. Patients and individuals living with pre-existing conditions often felt alone in evaluating their specific risks in relation to treatments and vaccines. In clinical settings, there was also a blurring of the line between treatment and research, and a lack of options apart from participation in research.

Experts from all workshops also offered advice for the drafting of the PREPARED Code. This included a recommendation that the code should not have a preamble describing the challenges that had been faced more broadly during the pandemic but could not be addressed by the main target audiences of the PREPARED Code, that is, researchers, research ethics committees or research integrity offices (see Sect. 8.5).

> To me, you need to make clear what the code is not about as well. A code which is about everything is useless. It means nothing anymore. You need to be really clear about what you're not talking about, and what you're not giving guidance on, and that might be a good content of the preamble. Not a preamble saying, "Hey, we needed to do that and that and that and we couldn't bring it in, so here it is." That doesn't make sense to me.
>
> Lex Bouter, Professor Emeritus of Methodology and Integrity, Vrije Universiteit Amsterdam.

After the workshops, summaries of the main themes were compiled from each session and sent to the participants in the form of a "validation workshop report" to ensure that discussions were captured accurately.

## 6 Values Mapping

Just like the TRUST Code, the PREPARED Code was intended to be values-based, so that the specific recommendations for research ethics and research integrity were linked to commonly understood moral values. Such a values-based approach creates a strong connection between *what* should be done during pandemics and *why* (morally) it should be done (Schroeder et al. 2019). Nevertheless, while the TRUST values of fairness, respect, care and honesty had resonated globally, their applicability to the PREPARED Code could not be taken for granted. Until the wide-scale research ethics and research integrity risks encountered during pandemics were identified, alignment of the challenges with the TRUST values was purely a matter of speculation.

As a starting point, the two analysts used the four TRUST values as a deductive framework for the analysis. They coded the research ethics and research integrity challenges independently: for each challenge they decided which of the four moral values was most at risk of being violated. The challenges to research ethics and research integrity that might be associated with more than one moral value were organised under the primary moral value at stake. To give the reader an idea of what this process looked like, here is an example.

A challenge from the PREPARED English-language report on research ethics and integrity challenges during COVID-19 was described as follows: "Researchers had to rely on ICU nurses and doctors to follow up enrolled participants on their behalf and share monitoring reports since they were not allowed to enter the ICUs."

To identify the values that this challenge illuminated, the analysts had to decide which moral values were being compromised or violated when researchers and ICU staff found themselves in these situations. In this case, it could be argued that both care and fairness were implicated. It was necessary for ICU nurses and doctors to collect data directly in order to protect patients and researchers from infection. Yet the additional workload and pressure on ICU staff could lead to stress and exhaustion, constituting a violation of the value of *care*. The same additional burden could also be interpreted as a violation of the value of *fairness*.

During this stage of the analysis, it was vital to ensure that the analysis remained grounded in the data to assess which was the main value at stake. For this example, both analysts deemed "fairness" to be the most important value at stake, due to the unfair burdens of data collection on ICU healthcare staff. Any disagreements between analysts were resolved through discussion with input from the lead author.

Additionally, the analysts remained open to the possibility that some challenges might be related to different moral values. For example, the moral value of *solidarity* has been described as important in guiding a global pandemic response (Dawson et al. 2020; Tomson et al. 2021), and it was reasonable to expect that solidarity might be required in a moral values framework that governs pandemics. However, while the relevance of solidarity to a small number of the risks was evident, these risks were deemed primarily matters of fairness and/or care. In fact, some scholars and commentators view solidarity and fairness as two closely related moral values of the same group, rather than clearly distinct entities (Küçük 2016; European Commission 2020; Cappelen et al. 2021).

Further, given the inclusion of research integrity challenges, more specific research integrity-related values such as accountability (ALLEA 2017) were also considered. But

accountability did not represent the *main* value at stake for any risk identified from the real-world challenges; there were no specific risks related to accountability that were not already represented by the values of honesty and fairness. While accountability might not be intuitively understood as falling under these values, it is contingent upon the honesty of the person being held to account and *may also involve some type of justice or fairness*[1] (Chatfield and Law 2024).

Thus, it soon became clear, during the process of mapping values for the PREPARED Code, that *all* of the identified pandemic-related challenges for research ethics and research integrity could be aligned with at least one of the four TRUST values. In other words, the identified breaches of research ethics and research integrity that emerged or were exacerbated during pandemics could all be associated with lapses or failures in fairness, respect, care and/or honesty.

In total, 160 challenges were identified and mapped to the TRUST values. Of these, 39 (24%) related to fairness, 29 (18%) to respect, 74 (46%) to care, and 18 (11%) to honesty (see Fig. 2).

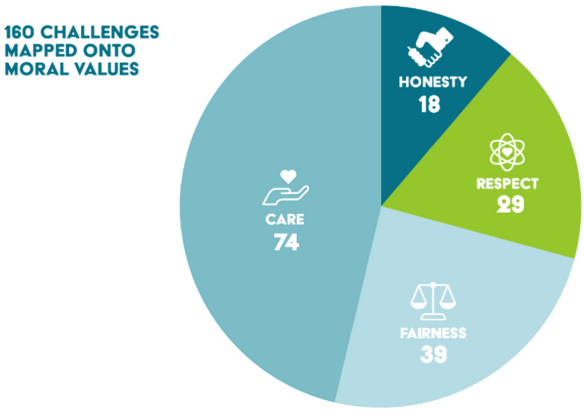


**Fig. 2.** Challenges mapped onto moral values

## 7 From Challenges to Risks

The next step of analysis entailed translating the reported challenges into descriptions of the potential *risks* for research ethics and research integrity during pandemics. This step also involved identifying the parties that might be affected by those risks (e.g. research participants, medical staff, research ethics committees and researchers). Again, this was undertaken independently by the two analysts and then compared and agreed through in-depth discussion with the lead author.

[1] For instance, distributive justice (fairness in distribution), procedural justice (being treated fairly), retributive justice (a correction or punishment) or restorative justice (to right a wrongdoing).

First, similar challenges were grouped together, for example this challenge from the literature review in English: *Minimising risks was difficult to guarantee due to lack of preliminary data on the investigational agents or approved drugs* (Kadam et al. 2022), and this one from the review in Mandarin: *A project wanted to study an antiviral drug, but action targets for experimental drugs did not exist in coronavirus* (Zhang et al. 2020). Both describe challenges associated with the testing of new interventions for a novel disease. For research ethics, this poses a risk to the consent process because participants should be informed about the potential harms and benefits involved before they decide whether to participate in a study. In other words, during pandemics, there can be a risk to the consent process if there is uncertainty about the disease and/or potential treatments (Article 11 in the PREPARED Code).

Secondly, once the challenges had been grouped, the risks were described in terms relevant to research ethics and/or research integrity, together with the parties that might be affected. For illustrative purposes, Tables 3, 4, 5 and 6 present selected examples of the risks we identified, those affected by the risks and the main moral value at stake in each case.

**Table 3.** Illustrative examples of *fairness* risks during global health crises

| FAIRNESS | |
|---|---|
| Risks for: | |
| Research participants | Unfair burdens when participating in poor quality studies that had no possibility of benefit |
| Society | Unfair exclusion of certain groups from studies meant that there were gaps in the evidence/interventions not tested for these groups |
| Research ethics committees | Unfair burden due to:<br>• Increased number of studies<br>• Pressure for rapid review/turnaround<br>• Other work pressures (many in healthcare)<br>• Fewer people available to undertake reviews<br>• Switch to alternative ways of working (e.g. online methods) which can be problematic for some |
| Healthcare staff | Unfair additional burdens for ICU staff who had to help with data collection and monitoring |

With the risks to research ethics and research integrity having been identified, it was now possible to start drafting the PREPARED Code.

## 8 Creating the First Draft

After 18 months of evidence-gathering and analysis, it was time to develop the first draft of the PREPARED Code.

**Table 4.** Illustrative examples of *respect* risks during global health crises

| RESPECT | |
|---|---|
| Risks for: | |
| Research participants | Consent issues (a selection):<br>• Research ethics committees did not have the necessary information for evaluation of risks and consent procedures<br>• Consent processes had to be adapted (e.g. proxy and e-consent) with unknown impacts<br>• Consent possibly compromised due to accessibility challenges with very sick patients in isolation |
| Society | • Many institutions did not comply with reporting and data-sharing obligations<br>• Lack of respect for opinion of experts<br>• Lack of compliance with research ethics norms and requirements |
| Research ethics committees | Lack of respect for REC authority, opinions and decisions |

The first draft was written by the lead author. The initial individual effort allowed for a consistency of voice as had proven beneficial during the development of the TRUST Code (Schroeder et al. 2019). Reducing a large number of specific risks to a smaller number of succinct articles was achieved by applying four steps of synthesis (see Fig. 3):

- focusing on the pandemic context
- tailoring results to target audiences
- grouping the risks so that several could be addressed through one article
- examining the depth of specificity.

### 8.1 Focusing on the Pandemic Context

Thousands of ethics codes already exist. In fact, the PREPARED team analysed 236 new ethics guidance documents for COVID-19 alone (See Chap. 4). With this proliferation of ethics documents in mind, the PREPARED Code authors aimed to develop a short, jargon-free code tailored to a particular situation, namely the next pandemic. One way of keeping the new code short and focused was to avoid the inclusion of recommendations that were already addressed in other widely adopted ethics and integrity guidance instruments. The PREPARED Code is designed to be complementary to other well-established codes. Indeed, some, like the TRUST Code, are cross-referenced because they are also relevant to pandemic times.

The risk of ethics dumping (the export of unethical research practices from higher- to lower-income countries (Schroeder et al. 2018) was identified in several of the literature reviews for the PREPARED Code. However, recommendations related to ethics dumping are already described in the TRUST Code: A Global Code of Conduct for Equitable Research Partnerships (TRUST 2018). Furthermore, the TRUST Code was developed by a group that consisted, in the main, of teams from low- and middle-income countries,

**Table 5.** Illustrative examples of *care* risks during global health crises

| CARE | |
|---|---|
| Risks for: | |
| Research participants | Potential harm from:<br>• Pressured research ethics committees which may not have time for due diligence<br>• Face-to-face interactions (infection risk)<br>• Receiving placebo (in placebo-controlled studies)<br>• Participating in human challenge studies<br>• Data breaches due to modified informed consent collection procedures (e.g. remote digital consent)<br>Unnecessary burdens from:<br>• Lack of coordinated studies<br>• Flawed study designs<br>Potential for therapeutic misunderstanding when rushed during consent process |
| Society | Reduced trust in science from:<br>• Misinformation and/or sensationalist reporting<br>• Failure to ensure quality and retract questionable publications |
| Research ethics committees | Potential for harm or stress from:<br>• Pressures to review quickly<br>• Resource shortages<br>• Switch to remote working |
| Health care personnel | Increased burdens because only they could access participants in ICUs |
| Animals | Potential for harm if regulatory reviews not carried out or not carried out effectively |

**Table 6.** Illustrative examples of *honesty* risks during global health crises

| HONESTY | |
|---|---|
| Risks for: | |
| Research participants | • Lower data protection standards in crisis situations<br>• Research participants not informed about use of their data<br>• Patients not informed about collection and use of samples |
| Society | Promotion of drug based on flawed or unverified information |

thus achieving appropriate representation on the topic (Schroeder et al. 2019). It was therefore decided to cross-reference the TRUST Code rather than add guidance articles tackling ethics dumping to the PREPARED Code.

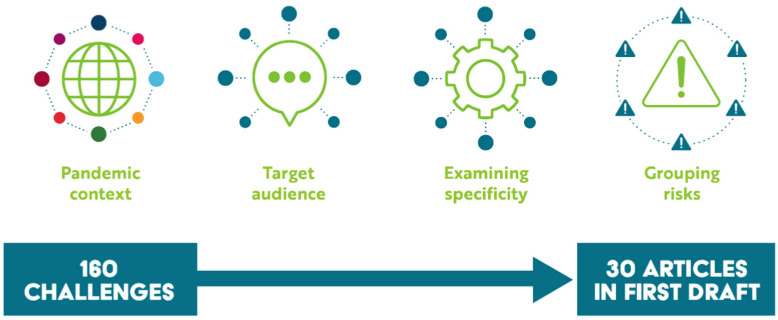


**Fig. 3.** Four steps of synthesis

### 8.2 Tailoring to the Target Audience

An ethics code is best aimed at individuals from a defined group; it will help those individuals undertake particular activities ethically through written guidance (Giorgini et al. 2015). The PREPARED Code is primarily aimed at researchers, and secondarily at research ethics committees and research integrity offices. The latter two *assist* researchers in undertaking their research ethically. Hence, they can also benefit from ethics codes in their advisory roles. This meant that some of the risks did not need to be addressed by the code's drafting team, as they were not relevant to these groups.

For example, resource shortages experienced by research ethics committees are an institutional issue that cannot be resolved by researchers alone. The fact that poor-quality publications remain in the published domain due to inaction by (predatory) publishers is not within the realm of researchers' influence (Barrière et al. 2023). Vaccine availability for lower-income settings is also not something researchers can readily address (Schveitzer and Thome 2021). It requires action at international level.

Because ethics deals with messy social worlds, it is not always possible to develop distinct categories, so there are four cases where the PREPARED Code refers to challenges that are not fully within researchers' power. These references were included because researchers can carry some of the responsibility for these aspects, and the PREPARED team decided to promote awareness of them.

First, the lead author added a vision statement to the code to make clear that all code authors believed firmly that questions of global access to vaccines were crucial in pandemic ethics, even though this was not the responsibility of researchers: *"Pandemic research should be trustworthy and the results accessible to all."* In this way the code at least acknowledges prominently the intractable problem of making vaccines accessible to all.

Second, two articles address research ethics committees *directly*. Article 7: "*RECs should expedite the evaluation of research proposals that address urgent societal needs without compromising rigorous ethical standards.*" Article 21: "*During pandemics, researchers may experience a heightened risk of hostility and related safety and security concerns. Research ethics committees should check that risk management plans are*

*in place*." This explicit guidance to research ethics committees was intended to provide an additional level of protection for researchers, in response to ample evidence of heightened safety and security risks to them during COVID-19.

Third, Article 15 stipulates: "*Especially during pandemics, researchers who handle potentially infectious biological materials should be adequately trained and equipped to safeguard public health.*" One could argue that getting staff trained is exclusively an institutional responsibility. However, successful training also requires good time management and motivation on the part of employees, and hence it was added to the PREPARED Code as a partial responsibility for researchers.

Fourth, two further articles might be considered beyond the power of researchers to implement: namely, Article 2, on coordinating research and avoiding wastage, and Article 4, on continuing community engagement during a major crisis. Indeed, both require multiparty involvement. Nevertheless, they were included in the code because researchers are not completely powerless in these areas. For instance, collaborating with as many colleagues as possible rather than trying to recruit to multiple small studies is something that researchers can consider. More obviously, successful community engagement is best driven by research teams. Hence, these two articles were included to raise researchers' awareness of the role they can play.

### 8.3 Grouping Risks

A synthesis step, which reduced the number of potential articles considerably, was the grouping of risks. The effect of this was to consolidate the ten risks relating to informed consent which had been identified in the literature reviews and subsequent values analysis into just three articles focused on consent in the PREPARED Code (Articles 9–11). For the purpose of precision and focus, this smaller number of articles addressed all the risks identified.

### 8.4 Examining the Depth of Specificity

Several of the literature reviews identified very specific research ethics challenges during a major crisis, for instance the most detailed and regularly cited ethical issues in human challenge studies (see Weijer 2024). The first version of the PREPARED Code included the following article: "During pandemics, healthy volunteers who take part in Stage 1 vaccine trials, carry risks and burdens for humankind. Researchers involved in such studies should follow the separate *Ethics Check List* for First-in-Human Vaccines."

The Ethics Checklist cited was also drafted by the lead author based on substantial work undertaken by the VolREthics Initiative (Inserm 2022). The checklist included 11 precise checkpoints, such as: "In bioconfinement, access to facilities, which counteract feelings of isolation, must be provided to ensure continuous wellbeing (for example, wifi, phones, TV, space, windows)," or "When offered, completion bonuses should be modest." This level of specificity would have been inappropriate for the PREPARED Code.

### 8.5 Input from the Validation Workshops

Following the consolidation work described above, the lead author formulated short articles in the format of ethics code guidance and checked whether the resulting draft code was compatible with the challenges, risks and suggestions identified in the report from the validation workshops (see Sect. 5).

One important decision had already come out of the validation workshop with research integrity experts. The PREPARED Code has no preamble, but merely a small number of introductory sentences (see Sect. 5). At first the lead author was keen on a preamble to distinguish the broader ethics issues identified in addition to the more specific research ethics and integrity issues. However, it was argued in this validation workshop that a preamble would reduce clarity by conflating different challenges. This idea was therefore dropped in favour of a single-sentence vision statement.

The validation workshops also unearthed one topic that was not raised in any of the nine language reports: benefit-sharing. While the compatibility of COVID-19 virus sharing (samples and genome) with the requirements of the UN Convention on Biological Diversity (CBD) and national biodiversity laws was discussed in the literature (Humphries et al. 2021; Sett et al. 2022), the pandemic *research ethics* literature we reviewed did not mention the topic. And as the CBD only covers non-human genetic resources, the CBD-related literature was not relevant to the coronavirus responsible for COVID-19.

In line with the vision statement, justice considerations formed a major part of ethics discussions during and after the COVID-19 pandemic, as was also emphasised by several delegates at the validation workshops. The lead author therefore agreed that a new article should be included in the code, which is now Article 3: "*A fair plan for access to the benefits of pandemic research should be agreed early on in any project, in collaboration with stakeholders.*"

### 8.6 Completing the First Draft

Progressing from the identified risks to a draft code of 30 articles took the lead author six weeks. This draft was then checked by the second author, Kate Chatfield, who suggested refinements across all topics. Following that check, it was sent to Natalie Evans for a focus on research integrity, to Pamela Andanda for a focus on Global South applicability and to Joshua Kimani for a focus on the adequate representation of the interests of persons in highly vulnerable situations.

At the same time, the draft including the refinements by the second author (Version 2) was sent to three external advisers, Prof. Fatima Alvarez-Castillo in Manila, Prof. Jantina de Vries in Cape Town and Prof. Charles Weijer in London, Canada. They were kind enough to provide video feedback in advance of the Amsterdam meeting (see Sect. 9.1). Here are examples of changes made in response to useful adviser input:

- The order of articles within each moral value was revisited to align with the steps in the research process.
- The phrase "with adequate protections" was added to Article 5, which deals with the inclusion of persons in vulnerable situations in research.

- The excellent phrasing about communicating risks and benefits "in terms of what is known, what is uncertain and what is unknown" in Article 11 was suggested by Charles Weijer.

## 9 Broad Consultation and Refinement

The PREPARED Code went through 13 iterations before it was finalised. Going from Version 1 to Version 13 involved disseminating the draft code as widely as possible to gather a wide range of perspectives and feedback.

Consultation formats differed, but all allowed for general feedback and comments on five specific questions:

1. Are the articles clear and understandable?
2. Can the ordering of articles be improved?
3. Is each article under the right value?
4. Do all disciplines feel covered?
5. Have we omitted anything important?

### 9.1 The Amsterdam Meeting

In its second draft, and accompanied by three videos from external advisers, the code travelled to Amsterdam for the opening of the consultations. At an in-person meeting of the PREPARED team partners and advisers (51 experts) in May 2024, input was collected via group discussions focusing on research ethics, research integrity and global relevance (Fig. 4).

**Fig. 4.** Group discussing the global relevance of the draft PREPARED Code, Amsterdam 2024

This round of expert feedback helped the lead author refine the code's articles and their relevance and applicability to the target groups of researchers, research ethics committees and research integrity offices. Also addressed were matters of content and format.

For instance, regarding content, there were discussions about what to do with risks that would require action *before* the next pandemic. The team considered the options of providing additional "resilience" or "preparedness" recommendations as part of the code, or of developing and referring to additional preparedness guidance. In the end, the team chose the latter option, to help keep the code short and jargon-free and to make it easier to update additional preparedness resources.

Regarding format, the meeting discussed the order of the values of fairness, respect, care and honesty in the code. Most of the Europeans in the group wanted *care* to be addressed first in the PREPARED Code, while the majority of the global team wanted *fairness* first. The final PREPARED Code starts with the value of fairness.

### 9.2 Dissemination to External Stakeholders

Wider dissemination of the PREPARED Code to stakeholders started around a month after the Amsterdam meeting, so there was time to refine the code in the light of the suggestions made at the in-person meeting.

The first external groups to be contacted for consultation were those already established via the PREPARED "stakeholder platforms". These had been formed during the time of evidence-gathering, led by consortium partners, to represent important networks of research stakeholders (Fig. 5). The platforms lend PREPARED the credibility, and the global reach, to solicit valuable comments from the right people on continuously refined drafts of the PREPARED Code.

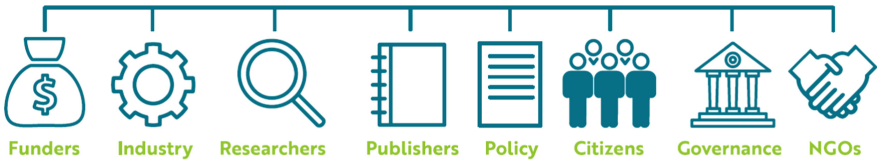


**Fig. 5.** PREPARED stakeholder platforms

In addition to circulating the code to platform members, the PREPARED team organised a wide range of activities from June to November 2024 to seek feedback from the following groups:

- experts working at the level of research ethics and research integrity policy and practice nationally (e.g. members of EUREC, the Forum for Ethics Review Committees in India and ENRIO) and internationally (e.g. members of the International Bioethics Committee of UNESCO and the World Commission on the Ethics of Scientific Knowledge and Technology)
- experts in specific areas of research ethics (e.g. experts in early-stage clinical trials and senior pharmaceutical industry bioethicists)
- researchers and students in relevant disciplines (e.g. metascientists, law and education researchers, and emergency ethics experts).

The public were also invited via a social media campaign to submit comments on the PREPARED Code via the PREPARED website in October and November 2024.

### 9.3 Considering and Responding to Comments

Between May and December 2024, the PREPARED Code went through 13 revisions. Most changes were triggered by feedback from the consultation activities, but some arose from further internal work by the PREPARED consortium.

For all potential revisions, the following criteria were applied:

- Proposed changes had to meet the four criteria from the synthesis process outlined above, that is, focusing on the pandemic context, tailoring results to target audiences, avoiding a proliferation of articles by combining issues, and avoiding overly deep specificity.
- Suggestions for changes had to be accompanied by evidence that a real-life challenge was involved.
- Suggestions that might be difficult to apply globally were to be avoided to ensure that the code would be useful around the world.

For consistency in decision-making, the lead author was responsible for the final version of all articles (in collaboration with a professional language editor). However, she convened small, fast-action, often ad hoc groups for many discussions to obtain further input and help her arrive at well-reasoned decisions. These small groups were usually needed after suggestions from external consultations. In addition, all changes were approved by the second author and, in the final instance, by all 57 authors.

## 10 Examples of Refinements Following Feedback

Below are four concrete examples of refinements arising from different types of consultations.

### 10.1 Written Consultations Through the Eight PREPARED Stakeholder Engagement Platforms

Several of the consultations with the platforms were undertaken in writing. Some feedback resulted in changes including the following:

- Consultation with industry (bioethics colleagues from Roche and Novartis)
  - The term "promptly" was added to Article 23, which requires researchers to inform participants and research ethics committees of changes in the risks or burdens of participation in clinical research.
  - The term "study suspensions" was replaced with the term "study modifications" in Article 18. This way, the impact on all those who depend on research studies for access to medication and services must be considered during a pandemic, not just the impact on those whose studies have been suspended.
  - The term "deception" was added to Article 27 about public communication by researchers.
- Consultation with the research integrity platform

– The phrase "or their proxies" was added to Article 9 about informed consent, given that not all research participants will be in a situation to make decisions for themselves during a pandemic.

### 10.2 In-Person Consultations at Conferences or Through Webinars

Some consultations were run as conference presentations or through webinars. At the ENRIO research integrity conference in Prague, an entire session was dedicated to feedback on the PREPARED Code, resulting in changes that included the following:

- The term "study limitations" was added to Article 27, which addresses how and what researchers should communicate publicly. In addition, to reduce jargon, the term "veracity" was removed from the article.
- The phrase "To promote public trust" was removed from Article 26, which asks researchers to answer publishers' research ethics questions. It was regarded as an unfounded deduction.

### 10.3 Gap Analysis

The risk-based approach of the PREPARED Code (see Chap. 3) demanded that research and consultation input inform every single article of the code. However, the PREPARED team also consulted existing ethics guidance, identifying research ethics and integrity challenges covered in existing COVID-19, Ebola and avian flu guidance (see Chap. 4). But, instead of simply incorporating challenges from existing guidance into the PREPARED Code, Vilma Lukaševičienė, who had undertaken the analysis of existing ethics guidance, compared the challenges she found with the articles in the draft PREPARED Code, a process that resulted in a small number of refinements, rather than new articles, including the following:

- "Quality controlled" was added to Article 1, which deals with the sharing of data about new infectious agents.
- "Health care responses" was modified to read "public health responses" in Article 14, which requires that such responses not be compromised by research.

### 10.4 Public Consultation

Public consultation was opened for seven weeks at the very end of the process, when the team had reached Version 12 of the PREPARED Code. Only one change was made in response to the public consultation, namely:

- The term "actors" in Article 12 was replaced with "all those involved in the research cycle".

### 10.5 The Final Draft

The handful of examples provided here give an indication of the level of consultation that led to Version 13. But they do not fully demonstrate how scrupulously every word in every article of the code was weighed. The most time-consuming element of the

consultation process for the lead author was giving feedback, which she provided in writing to explain why suggestions might fall outside of the scope of the code. What was surprising was that the substance of the code changed little from Version 1 to Version 13, which is probably thanks to the comprehensive research foundation on which the first draft had been built.

## 11 Lessons from the PREPARED Code Approach

Writing the PREPARED Code was a massive undertaking: time-consuming, costly and complex, as summarised in this chapter. However, ensuring that a swift research response during pandemics is undertaken ethically is an aim worth investing in. By showing the depth of effort that went into the creation of the PREPARED Code, we hope we have helped demonstrate its credibility. As noted in Chap. 3, it is the behind-the-scenes *process* of code development that confers credibility (Messikomer and Cirka 2010).

Fairness and inclusivity guided the methodology in terms of evidence gathering in multiple languages, the inclusion of marginalised groups through sensitive and appropriate methods, the recruitment of global experts and stakeholders to the validation workshops, and the numerous rounds of consultation and feedback which ensured the refinements necessary to move from Version 1 to Version 13 of the code. Indeed, the PREPARED team engaged in dialogue with as many groups affected by the code as possible, and stimulated dialogue between these groups.

Through listening to the experiences and perspectives of a global sample of research stakeholders, the PREPARED team was able to develop a code that all stakeholders in the research process can reasonably accept. Furthermore, the risk-based approach, which focuses on real-world challenges, provides an important reality check. A major strength of the approach is that the ethical requirements are rooted in real-world risks drawn from diverse voices and experiences. It is worth noting that the risk-based approach avoids two potential problems: first, that something might be included in a new code simply because it was included in another ethics code, and second, that something might be included in a new code merely because guidance drafters *believe* it to be a problem.

The first problem – that of a requirement being transferred from another ethics code – can lead to ethics codes that are misaligned to their audience, because almost all early ethics codes were focused solely on biomedical research. New ethics codes might consequently be based on a codification of a particular type of research (i.e. biomedical research) that then imposes its ethics requirements on different types of research *inappropriately* (Yanow 2008; Schrag 2011).

The second problem – drafters including articles *they* think are necessary – can lead to a misalignment with the real problems researchers are likely to encounter. As the PREPARED team's approach of building all ethics guidance articles *solely* on real-world problems is unusual, an analogy can perhaps best illustrate this point.

The history of research ethics guidance shows that the vast majority of initiatives and guidance documents were driven from the standpoint of high-income countries (Resnik and Hofweber n.d.). At the same time, research has shown that research ethics committees from high-income countries can impose "remote paternalism" on researchers and research participants from lower-income countries (Schroeder et al. 2024: 32). One

can therefore reasonably assume that there is a potential risk of misalignment between what ethics guidance drafters *think* are the challenges research ethics should seek to prevent and what these challenges really are, especially in a globalised world.

The values framework reflected in the TRUST and PREPARED Codes can be seen as a commitment to values that are commonly held globally and across cultures. While the methodology described above provided the space for other values to be identified, the final values of the PREPARED Code mirror the TRUST values of fairness, respect, care and honesty.

The approach is not, however, without limitations. The first draft of the code was developed after 18 months of research by a global consortium. This process was time-consuming and costly, requiring significant funding from the European Union, UK Research and Innovation and the Swiss State Secretariat for Education, Research and Innovation to implement. Such funds are not always available, which means that other groups might be unable to follow our approach on affordability grounds.

While we realise that not all initiatives will have access to the same resources, we hope to inspire groups tasked with developing professional codes of conduct in future to build their guidance on real-world problems and to be guided by the principles of fairness and inclusivity, making special efforts to involve the least privileged in decisions affecting our common futures.

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