adds, but anonymous accounts continue to tweet malicious things to her. She says it is unclear whether these are related to her posts about papers by Raoult and Chabriere.

Raoult and Chabriere's lawyer says that neither researcher, nor their institution, wishes to comment about the allegations in the letter.

Co-organizer of PubPeer Boris Barbour, a neuroscientist at the public-health research institute IBENS in France, is also named in the criminal complaint. Barbour declined requests for comment from *Nature*'s news team. A spokesperson for PubPeer told *Nature*: "A successful legal action could have a chilling effect on post-publication peer review."

"Direct legal action against the site has never been initiated," the spokesperson notes. "However, we have in the past resisted a subpoena seeking to identify our users, and PubPeer does occasionally receive and respond to legal threats."

Nature contacted ten journals that published papers authored by Raoult that have been flagged by Bik on PubPeer, including two papers about hydroxychloroquine and COVID-19, which he co-authored with Chabriere. Two of the journals say they have a policy of not commenting on such cases, and one says that no concerns have been raised about the paper in question. However, one of the papers flagged has since been retracted, one has had an erratum published and two others are under investigation.

Bik says she wonders why Raoult has not responded to specific concerns she raised about the papers. "Why doesn't he show me proof that I am wrong? I would be happy to accept that," she says. She adds that she has tried to not be hesitant about raising concerns on PubPeer in light of the case. "I don't want to be threatened. If I have broken the law, I would stop," she says. "But I have not."

LIMIT ON LAB-GROWN HUMAN EMBRYOS DROPPED

International stem-cell society relaxes the influential 14-day rule in its latest research guidelines.

By Nidhi Subbaraman

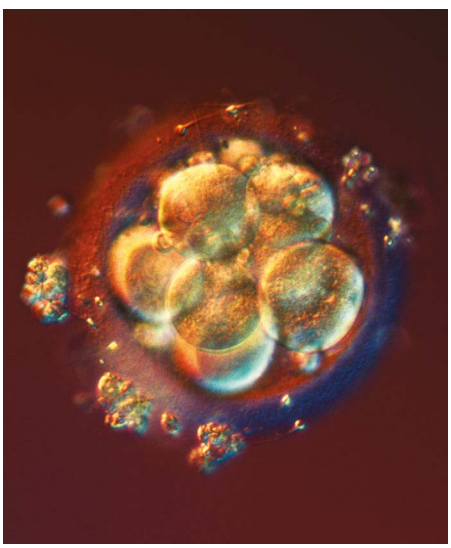
The international body representing stem-cell scientists has torn up a decades-old limit on the length of time that scientists could grow human embryos in the lab, giving more leeway to researchers who are studying human development and disease.

Previously, the International Society for Stem Cell Research (ISSCR) recommended that scientists culture human embryos for no more than two weeks after fertilization. But on 26 May, the society said it was relaxing this prominent limit, known as the 14-day rule. Rather than replace or extend the limit, the ISSCR now suggests that studies proposing to grow human embryos beyond the two-week mark be considered on a case-by-case basis, and be subjected to several phases of review to determine at what point the experiments must be stopped.

The ISSCR made this change and others to its guidelines for biomedical research in response to rapid advances in the field, including gene-editing innovations.

"It's been a major revision," says Robin Lovell-Badge, a stem-cell biologist at the Francis Crick Institute in London and chair of the ISSCR steering committee that wrote the new guidelines.

Last revised in 2016, the document offers a rubric for what science the biomedical community agrees is worthy, and which projects are off-limits.



LENNART NILSSON, TT/SPL

Scientific advances have made it possible to grow human embryos in the lab for weeks.

In the United States, where biomedical research involving stem cells or human embryos has been controversial for decades, and federal support has waxed and waned, the guidelines carry unusual weight, says Josephine Johnston, a bioethicist at the Hastings Center in Garrison, New York. Although US agencies have some policies covering such work, review committees at institutions or private funders often turn to the ISSCR's document as the only regularly updated set of guidelines representing the views of the scientific community. "That means that when they make a change like this, it is actually fairly significant," says Johnston.

The 14-day rule

First proposed in 1979, the 14-day rule bars research on embryos after they reach a key point of complexity. At least a dozen countries, including the United Kingdom, Canada and South Korea, have adopted the concept as law. Others, including the United States, have accepted it as a standard that guides researchers, reviewers and regulators.

With the new ISSCR recommendations, Lovell-Badge envisions that the longer a researcher wants to culture an embryo for, the tougher the country's regulatory authorities would have to make the review process. "We're not simply giving green lights for people to do this research," he says. Furthermore, the guidelines say that public comment should be part of the review.

Before 2016, researchers weren't able to keep human embryos alive in a dish for 14 days, so the rule didn't bar any projects. But that year, two independent research teams announced that they had been able to grow human embryos in a dish for up to 13 days — they then terminated the experiments in accordance with the 14-day standard.

Such advances have led some ethicists and researchers to argue that the decades-old rule is antiquated and ripe for revision. Allowing embryos to grow past 14 days, researchers say, could produce a better understanding of human development, and enable scientists to learn why some pregnancies fail, for instance. The revised ISSCR guidelines are a prompt to begin conversations about when it would be valuable to grow embryos beyond 14 days, says Alta Charo, a bioethicist at the University of Wisconsin Law School in Madison, who was part of the ISSCR steering committee. "We didn't debate it before — now it's time to debate."

In the past decade, scientists have made increasingly sophisticated models of embryos from human stem cells, demonstrating one way to study human development while avoiding the controversial use of embryos from fertility clinics. Such embryo-like structures are too rudimentary to grow into a person, scientists say. But relaxing the 14-day limit would

allow researchers to compare them fully with real embryos, and test them as feasible stand-ins for research, says Lovell-Badge.

Not everyone agrees that the shift to the rule is justified. Kirstin Matthews, a legal and policy scholar at Rice University's Baker Institute for Public Policy in Houston, Texas, says there is unexplored science to be done with embryos that are two weeks or younger, and that given the public scrutiny of studies of human embryos, the ISSCR should have engaged the public while considering changes to the guidelines. "It doesn't feel like we've exhausted our knowledge in this space," she says.

Lovell-Badge acknowledges that the review and redrafting steps did not include public-engagement exercises, in part because of the cost and time involved. Also, an international public-comment period would probably receive varied responses from different jurisdictions, he says. "You'd have to make it a huge exercise, and we can't do that."

Shifts in genetic science

Some of the other key changes to the ISSCR's ethics guide reflect advances in genetics.

For example, the guidelines now describe terms under which mitochondrial-replacement therapy could be used in medical research. Some metabolic diseases are caused by genetic mutations in the mitochondria, the power generators in cells, which children receive from their mothers. In cases where a mother's mitochondria carry these mutations, doctors can now swap the nucleus from the mother's egg cell into a donor cell with healthy mitochondria, whose nucleus has been removed, before *in vitro* fertilization (IVF).

In 2016, US physician John Zhang announced that he had attempted such a procedure, and delivered in Mexico what news reports called a 'three-parent baby'. Since then, researchers in the United Kingdom have won approval to begin clinical trials of the method.

The ISSCR guide also weighs in on whether it's okay to edit the genes of human embryos or egg or sperm cells intended for implantation, and concludes that this science is still too risky. In 2018, scientists were alarmed by an announcement from Chinese biophysicist He Jiankui that he had used CRISPR–Cas9 technology to edit genes in human embryos that he then implanted in a woman's uterus, resulting in the birth of twin girls. Since then, other expert panels have debated how to regulate gene editing that introduces heritable changes. They have pointed out that the procedure, still fairly nascent, can cause unintended changes to genes and has other technical flaws.

The ISSCR allows that the concept might be valuable in the future, for scientifically defensible reasons, once the science has advanced. "As a matter of absolute principle, we do not say that heritable editing is absolutely wrong in every possible circumstance," says Charo.

HOLLIE ADAMS/BLOOMBERG/GETTY

A street in Bolton, UK, where COVID-19 cases caused by variant B.1.617.2 have been identified.

THE RUSH TO STUDY FAST-SPREADING CORONAVIRUS VARIANTS

Questions remain about how quickly B.1.617 variants can spread, and whether they can evade immunity.

By David Adam

Since the SARS-CoV-2 variant known as B.1.617 was first reported in India late last year, it has spread to dozens of other countries — including the United States, Singapore and the United Kingdom, where it has become dominant in some regions.

Researchers have identified three subtypes, known as B.1.617.1 (the 'original' B.1.617), B.1.617.2 and B.1.617.3, each with a slightly different genetic make-up.

They are now rushing to investigate these variants and work out how they might affect the trajectory of the pandemic in countries where they have gained a foothold. Key questions remain about how quickly the variants can spread, their potential to evade immunity and whether they cause more severe disease.

A lot of this research takes the form of standard epidemiology — confirming COVID-19 cases through testing, identifying the variants responsible for infections and cross-referencing these data to people's clinical symptoms and vaccination statuses. Scientists can also glean insights from genomic-sequencing data, identifying which mutations are present in the B.1.617 subtypes and comparing these with mutations in earlier variants whose behaviour is better understood.

More transmissible

"I look at individual mutations because they each have individual properties that we think might confer higher transmissibility," says Julian Tang, a consultant virologist at the Leicester Royal Infirmary, UK. Increased transmissibility — a measure of how quickly variants can spread from person to person — could accelerate outbreaks, which could put more pressure on health-care systems and counter-measures such as vaccination programmes. For example, the B.1.617.2 variant has mutations called 452R and 478K, which Tang says are linked to increased transmissibility. Both mutations alter the spike protein, which the virus uses to enter human cells.

Researchers have also been able to rapidly track the spread of B.1.617.2, because its genome contains a marker not present in B.1.1.7, a variant now established in the United Kingdom and many other countries. The presence of this marker — known as the 'S gene target' — can be seen in the results of some of the PCR tests used to confirm cases of COVID-19,