Correspondence

ISSCR guidelines fudge heritable human-genome editing

I note troubling inconsistencies in the revised guidelines for stem-cell research and clinical translation, issued in May by the International Society for Stem Cell Research (ISSCR; see *Nature* **594**, 18–19; 2021). These imply that, in time, research that involves making heritable changes to the human genome will be permitted.

On page 9, the guidelines divide research into review categories. Research that is "not allowed" is split into 3A ("currently unsafe", with no mention of ethics) and 3B ("lacks compelling scientific rationale or is ethically concerning"). Yet page 14 mentions ethics in both categories, and rebadges 3A as "currently not permitted" and 3B as "prohibited".

Heritable human-genome editing is explicitly designated 3A. But, depending on one's perspectives, and whether referring to page 9 or 14, it could just as legitimately be in 3B. There are sound arguments to support the view that research into heritable human-genome editing lacks a compelling scientific rationale and is ethically concerning. (See my 2019 book *Altered Inheritance*.)

Further, a survey last year found that 75 of 96 countries with policies on such research prohibit it; none of the 106 countries surveyed permits it (F. Baylis *et al. CRISPRJ.* **3**, 365–377; 2020). So why is reference to research that is "illegal in many jurisdictions" included in the 2016 guidelines and not in the 2021 guidelines?

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Don't abandon 14-day limit on embryo research

As supporters of human-embryo research, we are troubled by the recommendations from the International Society for Stem Cell Research (ISSCR) to allow some *in vitro* studies of human embryo-like entities beyond the 14-day limit (see go.nature. com/3gfkkw8 and *Nature* **593**, 479; 2021).

There are 4 compelling reasons for the 14-day limit. Its clarity leaves little room for misinterpretation. It corresponds to important biological events, including the beginning of ectoderm/neural progenitors. In marking the end of the possibilities of twinning or chimaerism, it is the start of a unique biological identity. There is no later relevant nexus of events.

The guidelines recommend instead case-by-case approval for integrated embryos that are based on stem cells. This would permit research up to the "minimum time necessary" for scientific questions deemed "highly meritorious" through a "rigorous review process".

We caution that these utilitarian objectives are limitless. Furthermore, the questions deemed "highly meritorious" can be addressed using *in vivo* murine or near human arimete models

non-human primate models. The ISSCR must offer more-compelling arguments for

abandoning the 14-day limit.

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Concern over use of the term Z-DNA

We are writing to express our concern over use of the term Z-DNA to describe a righthanded, double-stranded Watson-Crick helix that incorporates the modified base diaminopurine (also known as 2-aminoadenine; see *Nature* **593**, 181; 2021). This use of Z-DNA is, we contend, confusing to scientists and the general public.

Z-DNA is the long-established nomenclature for a left-handed DNA structure first detailed at atomic resolution in 1979 (A. H.-J. Wang *et al. Nature* **282**, 680–686; 1979). Z-DNA and Z-RNA have an essential role in regulating type I interferon responses and programmed cell death by necroptosis. In other contexts, Z-DNA produces genomic instability, resulting in evolutionary adaptations and also in diseases such as cancer.

There are many examples of DNA structures that incorporate unusual or modified bases, but there is no precedent for renaming a structure because of this characteristic. In our view, a term other than Z-DNA should be used to characterize such findings.

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Regulate waste recycling internationally

China's 2017 ban on several types of waste import, and subsequent bans by countries in southeast Asia, stimulated a global trade in plastic waste. I call for improvements in the system to optimize the environmental benefits of waste reuse.

Recycling accords with the principles of a circular economy (see Y. Geng *et al. Nature* **565**, 153–155; 2019). It can conserve resources, protect the environment and help to cut greenhouse-gas emissions (Z. Liu *et al. J. Environ. Mgmt* **287**, 112283; 2021). But poor infrastructure for waste reuse turns some countries – Turkey, for instance – into a dumping ground.

To encourage more countries to recycle global waste, the process needs to be better organized and must conform to a set of international standards and regulations. Setting up an international database would help stakeholders to identify various categories of waste for reuse. Distribution chains from waste exporters to waste importers could become more efficient, environmentally friendly and cost-effective if backed by proper technical support at both ends.

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