

Regulating the Creation of Novel Beings

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Introduction

Bill C-13, *An Act respecting assisted human reproduction*,² proposes to regulate various elements of the creation of novel beings. Though the bill is directed primarily at the techniques and processes of human infertility intervention, it is concerned secondarily with some aspects of human embryo experimentation. The bill thus deals with the circumstances under which chimera- and hybrid-making would and would not be permitted, where the hybrid or chimera is created in part from human biological materials.

In this brief commentary, I focus on the proposed regulation of chimera- and hybrid-making. I probe some definitional oddities in the relevant portion the bill, assess possible scientific rationales for creating transgenic beings from human genes and cells, and touch on ethical and legal aspects of regulating the creation of these sorts of novel beings.

I. Definitional Issues

Bill C-13 distinguishes between “chimeras” and “hybrids.” Creating either type of creature is, *prima facie*, prohibited under the bill, carrying a maximum penalty of a fine of \$500,000 and/or a prison term of 10 years (though the actual penalty assessed may be less severe). Section 3 of *Bill C-13* defines “chimera” as:

1. an embryo into which a cell of any non-human life form has been introduced;
or
2. an embryo that consists of cells of more than one embryo, foetus or human being.”

“Embryo”, as defined in s. 3, refers exclusively to human embryos:

“embryo” means a human organism during the first 56 days of its development following fertilization or creation, excluding any time during

which its development is suspended, and includes any cell derived from such an organism that is used for the purpose of creating a human being.

“Hybrid” is also defined in s. 3 and means:

- (a) a human ovum that has been fertilized by a sperm of a non-human life form;
- (b) an ovum of a non-human life form that has been fertilized by a human sperm;
- (c) a human ovum into which the nucleus of a cell of a non-human life form has been introduced;
- (d) an ovum of a non-human life form into which the nucleus of a human cell has been introduced; or
- (e) a human ovum or an ovum of a non-human life form that otherwise contains haploid sets of chromosomes from both a human being and a non-human life form.

Section 5(1)(i) prohibits chimera-making:

5(1) No person shall knowingly

- (i) create a chimera, or transplant a chimera into either a human being or a non-human life form;

Section 5(1)(j) prohibits hybrid-making:

5(1) No person shall knowingly

- (j) create a hybrid for the purpose of reproduction, or transplant a hybrid into either a human being or a non-human life form.

Are these definitions scientifically or legally adequate? Let us begin with hybrids. A vague definition of “hybrid” would not have sufficed, either legally or scientifically. An example of a vague definition is that provided by Genome Canada, and adopted from the Human Genome Project Information website: “The offspring of genetically different parents.”³ At least in the case of animals (including



humans), unless the parents are identical twins, they will be “genetically different.” A regulation prohibiting the creation of hybrids so defined would prohibit reproduction except – *per impossibile* – between identical twins!

Within the context of a bill concerning human reproduction and human reproductive materials, a scientifically adequate definition of “hybrid” (involving human genetic or cellular material) should capture at least the following possibilities: the fertilization of a human ovum with non-human sperm; the fertilization of a non-human ovum with human sperm; the insertion of a non-human cell nucleus into a human enucleated ovum; and the insertion of a human cell nucleus into a non-human enucleated ovum.

As written, the *Bill C-13* definition of “hybrid” does indeed capture these four possibilities – subsections (a)-(d) in the definition cited above. The *Bill C-13* definition is, however, more exhaustive, in that it contains as well a “catch-all” subsection – subsection (e): “a human ovum or an ovum of a non-human life form that *otherwise contains* haploid sets of chromosomes from both a human being and a non-human life form” (emphasis added). This fifth subsection captures possibilities for hybridizing human and non-human genomes not otherwise enumerated in the definition. Because the definition of “hybrid” employed in *Bill C-13* is clear and exhaustive, the bill’s prohibition on hybrid-making is thus very strong.

The same is not true, though, of the prohibition on chimera-making. For regulatory purposes at least appropriately defining “chimeras” is considerably more complex than appropriately defining “hybrids.” As noted above, the *Bill C-13* definition of “chimera” captures two possibilities: the insertion of non-human cells into human embryos, and the inclusion, within any single human embryo, of cells from other human embryos, human fetuses, or human beings. It is prohibited either to create such chimeras, or to implant them in humans or non-humans. This is a narrow definition of “chimera”; the narrowness of the definition provides for both potential advantages and potential disadvantages.

Among its potential advantages is its precision. A prohibition on the creation or implantation of chimeras so defined is clear: it is forbidden to knowingly add “foreign” cells to a human embryo by, for instance, fusing embryos, or to implant an embryo so manipulated.

A second potential advantage is that the definition does not include, for instance, organ recipients (through either

conventional or xenotransplantation) as chimeras. This is because the definition is restricted to the embryonic stage of human development. Other definitions of “chimera” are much more inclusive, and would require deeming transplant recipients to be “chimeras.”⁴ A prohibition based on a too-broad definition of “chimera” would forbid transplant surgeries – surely not the intent of the bill in question.

A third potential advantage is that the definition includes a “catch-all” clause – it does not detail which techniques are specifically prohibited, but rather includes all techniques for altering

human embryos through the addition of human or non-human cellular material.

What, then, are its potential disadvantages? The most glaring one is that the definition of “chimera” in *Bill C-13* does not capture the insertion of human cells into non-human embryos, or the implantation of a creature so created in a human or non-human life form.⁵ While the definition of “hybrid” (and the correlative prohibition) refers to both human-to-animal and animal-to-human combinations, the definition of “chimera” (and the correlative prohibition) refers only to animal-to-human and human-to-human combinations.⁶ So, according to *Bill C-13*, it is prohibited to insert non-human cells into human embryos (animal-to-human chimeras) or to insert human cells into human embryos (human-to-human chimeras), while it is not prohibited to insert human cells into non-humans (embryonic or otherwise – human-to-animal chimeras).⁷

In the *Proposals for Legislation*⁸ drafted in 2001, the proposed definition of “chimera” was considerably broader. Section 9(3) of the *Proposals* defines a “chimera” as “(a) a human embryo or foetus into which a cell of any non-human life form has been introduced; or (b) a non-human embryo or foetus into which a cell of a human being or of a human embryo or foetus has been introduced” – both animal-to-human (a) and human-to-animal (b) creatures are explicitly recognized in the *Proposals* (although the *Proposals* do not capture human-to-human combinations). The *Proposals for Legislation* differ in other important ways from *Bill C-13*.⁹ For instance, chimera-making is not prohibited in the *Proposals*, but rather regulated through licensing – see section 9(1). Moreover, there is no definition of “hybrid” in the *Proposals*; rather, section 9(2) of the *Proposals* stipulates the requirement of a license in order to legally

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undertake to combine the genomes of humans and non-human animals (which is distinguished in the *Proposals* from creating chimeras).¹⁰

Scientifically, there is no reason to draw a strong distinction among animal-to-animal, animal-to-human, human-to-animal, and human-to-human chimeras. A scientifically adequate definition of a “chimera” would be “an embryo”¹¹

containing a mosaic of (at least) two genomes, produced, e.g., via the mixture of embryonic cells from two or more species (or from two or more creatures of the same species) at an early stage of development.” Such a definition has all of the advantages of the definition contained in *Bill C-13*: it is precise, it would not define transplant recipients as chimeras, and it is exhaustive in the same way.

It is also, unfortunately, entirely inappropriate within a Bill concerning *human* reproduction. The definition proposed in the previous paragraph is inclusive of human-to-animal, human-to-human, animal-to-human, and animal-to-animal combinations. But as the drafters of *Bill C-13* were no doubt well aware, a bill concerning *human* reproduction should not regulate animal-to-animal combinations. Despite its scientific adequacy, then, this definition is over-inclusive for legal purposes within *Bill C-13*.

However, by the same token, the definition of “chimera” in *Bill C-13* may be deemed legally inadequate, because it is under-inclusive in not capturing human-to-animal combinations, such as the addition of human embryonic stem cells to non-human embryos.

Presumably, a decision was made to restrict the definition of chimeras and the correlative prohibitions in *Bill C-13* to animal-to-human and human-to-human creatures; that is, the exclusion of human-to-animal creatures was presumably intentional, and not simply an error. If not – if it was, in fact, merely a mistake to exclude human-to-animal combinations – then remedying the deficiency of the *Bill C-13* definition is a quite straightforward matter.¹² If we assume, however, that the drafters of this legislation had reason to restrict the definition, then the legal and scientific aspects of the definition of “chimera” are independent (as is often the case in law): a “chimera” scientifically construed (as in the proposed over-inclusive definition above) is not the same as a “chimera” legally construed.

That said, that *Bill C-13* does not regulate the creation of animal-to-animal chimeras is entirely reasonable: it is a bill

concerning human reproduction, dealing with embryo research only where the embryos in question are human embryos. So we can easily understand the first legal restriction on the definition of “chimera”: animal-to-animal combinations are not, and should not be, covered.

But there is a second legal restriction of the definition of “chimera” within *Bill C-13*:

only animal-to-human and human-to-human creations count as chimeras (the creation

and implantation of which are prohibited). But why shouldn’t human-to-animal creations count, legally, within *Bill C-13*, as chimeras?

Scientifically, there is no reason to draw a strong distinction among animal-to-animal, animal-to-human, human-to-animal, and human-to-human chimeras.

II. The Ends of Transgenesis

An answer may be sought in a brief exploration of the goals of chimera research. Biomedical scientists justify the creation of novel transgenic beings (*without* using human cellular or genetic material) on a variety of grounds.¹³ A standard theoretical justification is that genetic manipulation (such as gene “knock-out” and “knock-in” experiments) permit ostensibly unambiguous interpretation of gene function in development.¹⁴ Another more practical justification is that transgenic organisms can be used to better understand and eventually to intervene in human development, both normal and, more often, disordered. Because chimeras and hybrids can be made to yield, quite consistently and reliably, the disordered phenotype of interest, they are putatively ideal models for increasing knowledge about disease states and aetiology. Of course, development is a remarkably complex affair in all creatures, and the relationship between genome and phenotype is virtually never linear.¹⁵ The justification for creating transgenic beings, though, is that such beings can illuminate particular aspects of biology in ways impossible (or at least supremely difficult) through non-transgenic research.¹⁶

That said, why should anyone want to create a hybrid or chimera using *human* cells?¹⁷ Recall the distinction among animal-to-human, human-to-human, and human-to-animal creations. *Bill C-13*, as it currently reads, prohibits the creation of all hybrids as well as the creation of animal-to-human and human-to-human chimeras, but permits (or at least does not prohibit) the creation of human-to-animal chimeras. It is quite straightforward to grasp the scientific rationale for creating human-to-animal beings (whether hybrids or chimeras): to facilitate the study of human biology, normal and disordered.

DNA sequences are widely conserved throughout the organic world. That is, the human genome contains DNA sequences that are present as well in a disparate variety of other genomes – chimpanzee, mouse, fruit fly, even rice and yeast. Comparative genomics research promises to yield new insights into the similarity between DNA sequences in these and other organisms.¹⁸ The mouse is standardly used as a model for research into human diseases; this is not only because mice have short generation times, produce large litters, and we have detailed knowledge of how to manipulate the mouse genome, but also because, in addition to sequence similarity, there is also some similarity of function between mouse genes and human genes. But biomedical researchers are not interested, for the most part, in studying *mouse* diseases; they want to investigate *human* diseases. Hence the desirability of transgenic mice, engineered with DNA from a human – such as a particular mutation believed to be involved in the aetiology of a human disease. The human DNA may in fact be very similar to the mouse DNA that it supplements or replaces. But there may also be important differences between the two stretches of DNA. A transgenic (human-to-animal) being may thus afford critical insight into gene expression and the development of the disorder. Clearly, though, there are distinct phenotypic differences between humans and mice, such that mice are not ideal model systems for humans: in the case of cystic fibrosis (CF), for instance, mice usefully model CF-related intestinal abnormalities, but “do not model the devastating lung disease of CF patients.”¹⁹ Accordingly, sheep, pig, primate, or other models may be sought for transgenic purposes.²⁰

A possible objection to this rationale for producing human-to-animal creatures is that it is difficult to extrapolate results from animal models to humans, just as it is difficult to generalize results from one species across all (or some) other species. The rejoinder would be that studying specifically human DNA within the context of a transgenic model system would remove some (even if not all) barriers to scientific inference (this is an empirical claim to be borne out or disconfirmed through additional research).

Given the scientific rationales summarized here, as well as the discussion of definitional issues in section I of this essay, I now attempt to assess the logic of this aspect of *Bill C-13*

III. Justifying Prohibitions

Let us begin by inferring two possible reasons for the change in the definition of “chimera” from the *Proposals for Legislation* to the final text of *Bill C-13*. One of these

reasons is based on science, the other on morality. I will address each in turn.

Given the analysis in section II of this essay, we can thereby infer that the empirical difference that makes for a legal difference in the further restriction of the definition of “chimera,” is that we can reasonably foresee biomedical benefits

But why should transgenic manipulation of the human genome be forbidden?

from the creation of human-to-animal chimeras; there is, though, no biomedical or scientific reason to create animal-to-human chimeras. Thus, we should not prohibit the creation of human-to-animal chimeras (in fact, according to *Bill C-13*, we should not even call them “chimeras”), while we should prohibit the creation of animal-to-human chimeras. That there is no scientific rationale for creating animal-to-human chimeras is a sound reason to prohibit such activity, while the existence of a scientific rationale for creating human-to-animal chimeras is a sound reason not to prohibit such activity.

But should a suitably compelling scientific rationale be presented for the production of human-to-human or animal-to-human chimeras, would these creations eventually be permitted (possibly with a license)? If the answer is no, then, presumably, the drafters of *Bill C-13* would explain that their definitional decision was informed by both scientific and extra-scientific factors.²¹

Scientific rationale thus plays an odd role in the definitions and prohibitions in *Bill C-13*. If science were all that mattered, then presumably the creation of all biomedically useful chimeras would be permitted. But science is not all that matters. What else matters, or should matter, and why?

Perhaps the drafters of *Bill C-13* were swayed by ethical arguments. If so, then we can tease out another reason for prohibiting the creation of animal-to-human and human-to-human chimeras: to guard against transgenic manipulation of “our” genome as the likely next step following on manipulation of the genomes of other creatures, including non-human primates. But why should transgenic manipulation of the human genome be forbidden? On what grounds might one argue the case? These are among the most difficult questions ever pondered by philosophers²² – but, aside from vague, unsubstantiated references to “human dignity” and “the integrity of the human genome,” no answers are forthcoming in the context of *Bill C-13*.

We know through *Bill C-13* what would be permitted and what would be prohibited should the bill become law. But we know virtually nothing, through *Bill C-13*, about why

making human-to-animal chimeras should not be prohibited, or why the creation of all interspecific hybrids involving humans, and the creation of human-to-human and animal-to-human chimeras should be prohibited.

The law need not justify legal definitions or prohibitions, which is eminently convenient in this particular case, because morally justifying the prohibition on some forms of chimera-making is no easy task. Nonetheless, philosophers and lay folk may well demand justification for both the permissions and prohibitions contained within *Bill C-13*; they will be disappointed to find no justification in the bill as it currently reads.

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2. 2d Sess., 37th Parl., 2002 (1st reading 9 October 2002), online: Parliament of Canada <http://www.parl.gc.ca/37/2/parlbus/chambus/house/bills/government/C-13/C-13_1/C-13_cover-E.html> (date accessed: 15 October 2002) [*Bill C-13*]. *Bill C-13* was re-introduced into Parliament pursuant to an Order made October 7, 2002, in the same form as Bill C-56, *An Act respecting assisted human reproduction*, 1st Sess., 37th Parl., 2002 (1st reading 9 May 2002), online: Parliament of Canada <http://www.parl.gc.ca/37/1/parlbus/chambus/house/bills/government/C-56/C-56_1/C-56_cover-E.html> (date accessed: 5 September 2002), which was prorogued at the close of the first session of the 37th Parliament.
3. Human Genome Project Information Glossary, online: Oak Ridge National Laboratory <http://www.ornl.gov/TechResources/Human_Genome/glossary/glossary_h.html> (date accessed: 12 September 2002).
4. Examples of such over-inclusive definitions are those offered in the report on stem cell research by the American Association for the Advancement of Science and the Institute for Civil Society (“An individual, organ, or part of an organism consisting of tissues of diverse genetic constitution”), and that provided by Lee and Morgan (“An individual consisting of cells or tissues of diverse genetic constitution”). See A.R. Chapman, M.S. Frankel & M.S. Garfinkel, *Stem Cell Research and Applications: Monitoring the Frontiers of Biomedical Research* (New York: American Association for the Advancement of Science and Institute for Civil Society) at 31, online: American Institute for the Advancement of Science <<http://www.aaas.org/spp/sfrl/projects/stem/report.pdf>> (date accessed: 14 September 2002); R.G. Lee & D. Morgan, *Human Fertilisation &*

Embryology: Regulating the Reproductive Revolution (London: Blackstone Press, 2001) at 386. Of course, “diverse” in these definitions may be interpreted more strongly than as “different”, but vagueness is nonetheless inherent in these definitions.

5. The discussion in this paragraph and the next draws heavily upon the work in progress of my colleague, Matthew Herder. I am grateful to him for sharing his thoughts.
6. In order to avoid interpretive difficulties, it is important to develop a convention regarding how to name chimeras. In this commentary, I employ the following convention: “human-to-animal” denotes the addition of human genetic or cellular material to a non-human embryo; “animal-to-human” denotes the addition of non-human genetic or cellular material to a human embryo; “human-to-human” and “animal-to-animal” are self-explanatory.
7. The creation of animal-to-animal chimeras is not within the purview of a bill regulating *human* reproduction, a bill in which “embryo” refers exclusively to “human embryo.”
8. Health Canada, “Proposals for legislation governing assisted human reproduction,” (Draft 2001), online: Health Canada <<http://www.hc-sc.gc.ca/english/pdf/reproduction/legislation.pdf>> (date accessed: 13 September 2002).
9. The differences between the *Proposals* and *Bill C-13* are noteworthy and deserve further scrutiny; here I shall focus only on the definitional differences.
10. Section 9(2) of the *Proposals* is almost identical to section 11(1) of *Bill C-13*; whereas in the *Proposals* the section is entitled “Combinations with animals,” in the bill it is entitled “Transgenics.” For a discussion of what might and might not be covered by section 11(1) of *Bill C-13*, see the article by Françoise Baylis, “Betwixt and Between Human Stem Cell Guidelines and Legislation,” in this issue.
11. “Embryo” is not the ideal word here, given Bill C-13’s equation of “embryo” with “human embryo”.
12. Of course, legislators may prefer to treat, as a matter of law, the creation of animal-to-human, human-to-human, and human-to-animal chimeras differently, even if they all count as chimeras: for instance, the creation of animal-to-human and human-to-human chimeras may be prohibited, while the creation of human-to-animal chimeras may be permitted (as is the case with *Bill C-13* as it currently reads, though the permissibility of human-to-animal chimeras is not entirely clear within the bill; at least, their creation is not prohibited); or the creation of human-to-human chimeras may be prohibited (or regulated by licensing), the creation of animal-to-human chimeras may be prohibited (or regulated by licensing), and the creation of human-to-animal chimeras may be permitted (a possible liberalization of *Bill C-13*). Alternatively, the creation of any chimera (animal-to-human, human-to-human, or human-to-animal) may be regulated by licensing (an alternative possible liberalization of *Bill C-13*), or prohibited altogether (a more conservative position than represented in *Bill C-13*). The latter would be much closer to the position represented in the CIHR guidelines, specifically sections 7.4.4-7: Canadian Institutes of Health Research, *Human Pluripotent Stem Cell Research: Guidelines for CIHR-Funded Research* (4 March 2002), online: Canadian Institutes of Health Research <<http://www.cihr-irsc.gc.ca/publications/ethics/>



stem_cell/stem_cell_guidelines_e.shtml> (date accessed: 19 September 2002).

13. Useful reviews are provided by R.M. Petters & J.R. Sommer, "Transgenic Animals as Models for Human Disease" (2000) 9 *Transgenic Research* 347; D.I. de Pomerai, "Are There Limits to Animal Transgenesis?" 3 *European Journal of Genetics in Society* 4; and R.S. Williams & P.D. Wagner, "Transgenic Animals in Integrative Biology: Approaches and Interpretations of Outcome" (2000) 88 *Journal of Applied Physiology* 1119.
14. I qualify this claim with "ostensibly" because knock-out experiments sometimes may be used as the basis of inappropriate inferences; for a discussion, see K.K. Smith & R.A. Schneider, "Have Gene Knockouts Caused Evolutionary Reversals in the Mammalian First Arch?" (1998) 20 *BioEssays* 245; see also J.S. Robert, "Interpreting the Homeobox: Metaphors of Gene Action and Activation in Development and Evolution" (2001) 3 *Evolution & Development* 287.
15. R.C. Strohman, "Epigenesis – The Missing Beat in Biotechnology" (1994) 12 *Bio-Technology* 156; see also J.S. Robert, *Embryology, Epigenesis, and Evolution: Taking Development Seriously* (Cambridge: Cambridge University Press, forthcoming).
16. Petters & Sommer, *supra* note 13; Williams & Wagner, *supra* note 13.
17. Here I focus exclusively on human-to-animal chimeras – the only sort of human-involving chimera not prohibited in *Bill C-13*. Though I believe there may be a justifiable scientific rationale for creating human-to-human chimeras, their creation is prohibited by the bill, suggesting that scientific rationale, though important, is not the deciding factor between permissible and impermissible research.
18. N.G. Copeland, N.A. Jenkins & S.J. O'Brien, "Mmu 16 – Comparative Genomic Highlights" (2002) 296 *Science* 1617; an enhanced version of this article, with hyperlinks to additional resources, is available online: *Science Magazine* <<http://www.sciencemag.org/cgi/content/full/296/5573/1617>> (date accessed: 6 June 2002); see also M.S. Lesney, "Ecce homology: A Primer on Comparative Genomics" (2001) 4.11 *Modern Drug Discovery* 26, online: ACS Publications <<http://pubs.acs.org/subscribe/journals/mdd/v04/i11/html/11lesney.html>> (date accessed: 15 September 2002), and D. Cyranoski, "Chimpanzee Genome: Almost Human ..." (2002) 418 *Nature* 910.
19. Petters & Sommer, *supra* note 13 at 349.
20. This would clearly be the case where transgenic technologies are used to reduce the rejection rate of xenotransplanted organs – raisin-sized mouse hearts just won't do for humans.
21. It is curious that, had the *Proposals for Legislation* been accepted, all forms of interspecific chimera-making involving humans would have been permissible, though regulated by a licensure system, while within the bill, despite the availability of the licensure option, the creation of two types of chimera (animal-to-human and human-to-human) is explicitly prohibited, while the creation of human-to-animal chimeras is implicitly permitted (though licensing may be required, depending on the regulations to be established at a later date). Why was the licensure option not explicitly pursued? Again, presumably, the answer is to be found in extra-scientific considerations, whatever those might be.
22. See J.S. Robert & F. Baylis, "Scientific and Moral Confusion About Crossing Species Boundaries" (2002) submitted.

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