



## LETTERS

Immigration and population growth are crucial to making Sweden's inbred wolf population sustainable.

Edited by Jennifer Sills

## Planned cull endangers Swedish wolf population

In May, the Swedish Parliament announced a goal to reduce the Swedish wolf population from about 400 to about 200 individuals (1). This action further threatens this highly endangered population, which is genetically isolated and inbred. Scientific advice for improvements has not been implemented (2, 3).

The Swedish Parliament proposed this drastic cull at a time when biodiversity is a global focus. The 50-year anniversary of the first UN conference on the environment was celebrated in June, and the UN Convention on Biological Diversity (CBD) will soon finalize its global biodiversity framework for 2020 to 2050. Sweden's actions are inconsistent with the country's obligations under the CBD and European Union law.

Few wild populations are as well studied as the Scandinavian wolf. Genetic monitoring has provided a full pedigree since the population was reestablished in the 1980s after extinction, and the data confirm persisting genetic isolation (4–6). Hunting, conducted both legally and illegally, has prevented population expansion and the influx of genetic variation.

Three founders comprised the population's genetic origin until 2007, and only three more wolves have subsequently contributed genetically to the present

population (6). The genetic base is thus extremely narrow, and genomic erosion has been confirmed (7, 8). The average level of inbreeding is similar to the level found in the offspring of two full siblings (6). Inbreeding in this population has been shown to reduce litter size (4). Also, high frequencies of anatomical defects (9) and male reproductive disorders (10) have been observed.

To make this population viable, population size and immigration must increase. So far, the population has been too small, and limited immigration followed by inbreeding could lead to extinction, similar to the Isle Royale wolf population (11). The goal should be to recreate a well-connected metapopulation spanning Scandinavia and Finland with a genetically effective population size of over 500, in line with the proposed CBD indicator (12). Considerably more genetic exchange than the current one-migrant-per-generation aim is needed (3).

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### COMPETING INTERESTS

This work is the view of the authors and not necessarily that of the agencies they represent.

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## End animal testing for biosimilar approval

Drug toxicology testing in animals has long been a standard requirement for establishing the safety of both new drugs (1) and copies of biological drugs coming off patent, known as biosimilars (2). Recently, the international community has acknowledged that this type of test may not be necessary or useful. Although policies for new drug approval are in the process of changing, biosimilar approval policies have been overlooked. Regulatory agencies should update these policies to streamline the biosimilars approval process and to prevent unnecessary, and thus unethical, animal testing.

Policies requiring animal toxicology studies to test biosimilars often stipulate the

use of a dose multiple times as high as the human dose (3). This strategy fails to recognize that higher doses lead to nonlinear responses, which invalidates the results. In addition, the animal species used in many studies do not have the binding receptors that the drugs target in humans, or they have similar receptors that bind to drugs at concentrations different from those in humans. Given the differences in receptors, either animals cannot respond or develop side effects to the drug, or their response lacks relevance to the human response (4).

The US Food and Drug Administration (FDA) is discussing alternative models of testing for new drugs (5, 6) but still requires animal toxicology studies for biosimilars (2). The requirement remains even though the FDA has discarded most of these studies, which are often conducted by the dozens for a single biosimilar drug (7, 8). The World Health Organization and other regulatory agencies [e.g., (3)] also still require animal toxicology studies for biosimilar approval (9). Only the European Medicines Agency (10) has updated its policy to reflect that animal pharmacology and toxicology studies are irrelevant to the evaluation of biosimilars.

More than 120 biosimilars have been approved in the United States and the European Union (7), and no results from the required animal studies have yielded useful information about responses or side effects in humans. It is time for regulatory agencies to forbid animal testing for biosimilar approval for the sake of animal welfare, cost, and time.

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#### LIFE IN SCIENCE

## Danger in the desert

Deep in Chile's Atacama Desert, a landscape often compared to Mars, our team of four female microbiologists watched as a car full of curious men pulled up beside us. Because we were strangers in a desolate place, our minds immediately jumped to ways we could protect ourselves. Defensively, our Chilean compatriot hefted the sturdy shovel she'd been using to dig up plant roots. The rest of us tried to look braver than we felt.

We had come to this desert to conduct DNA studies on giant horsetails, fern-related plants that somehow flourish in one of Earth's driest places. We were searching for plants in the most remote locations, where they would be unaffected by human activities such as mining and agriculture.

#### Call for submissions

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We'd been warned that the trip could be dangerous. Because we were traveling so far from fuel sources, we were told to take along a can of gasoline. Our destination was at the end of a tortuous single-lane dirt road lined with burned-out vehicles that had not successfully negotiated the steep descent. Our sample site was near a village, and the people, we were told, might not respond positively to us. We were instructed to report our travel plans at the nearest police station so that

search parties would know where to look for us if we disappeared.

We had found the amazing plants; their bright green stems towered over our heads, evoking thoughts of ancient Carboniferous swamp vegetation. The men approached as we finished collecting our samples. We waited tensely as a man exited the car and walked toward us. To our surprise and relief, he politely invited us to visit their village—they wanted to show us a lovely church of which they were justifiably proud. That day, we learned about more than the microbiomes that help desert plants thrive. We also met a welcoming community who had likewise beautifully adapted to their challenging home.

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The author's team negotiated remote roads deep in Chile's Atacama Desert.

