Policy and regulations in light of the human body as a ‘superorganism’ containing multiple, intertwined symbiotic relationships

Dillan Bono-Lunn, Chantal Villeneuve, Nour J. Abdulhay, Matthew Harker & William Parker

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ABSTRACT
The human body is now understood to exist as an ecosystem that includes an abundance of life, called the human biome. For purposes of understanding and treating disease, the biome of the human ‘superorganism’ can be divided into three parts: human, microbial, and more complex organisms such as worms and protists. This paper examines medical progress with biome restorative practices, including fecal microbiota transplants and helminthic therapy, which have proven in some cases more effective and more economical at treating a wide range of diseases than pharmaceutical-based approaches. The regulatory and policy hurdles responsible in part for this limited use of these restorative practices are examined. More importantly, new approaches are encouraged which might reverse the general lack of interest for these restorative practices seen in the medical and biomedical research communities. Such approaches include the regulation of benign helminths as dietary supplements and the establishment of an Institute of Health focused on biome-related issues. Further, the formation of humanitarian organizations to produce and distribute products for biome restoration should be encouraged by public policy, mirroring the collection and distribution of blood and blood products by the Red Cross and Red Crescent Societies.

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Introduction
It is now widely appreciated that the human body is much more than evolutionarily derived human DNA and the results of transcribing, translating, and replicating that DNA into the components of life. Rather, the human body consists of a vast array of organisms, each with its own evolutionary history and genetic material, which interact in intricate and as yet poorly understood ways to make a functional human organism.

The life associated with an ecosystem is called a ‘biome’. Like the biome of any ecosystem, the human body’s biome is complex, with intricately intertwined components. Our bodies naturally interact with yeast, viruses, bacteriophages (viruses that replicate in bacteria), protists, and helminths (worms that live in our gut). A wide range of factors associated with Western society has affected this diversity of life, depleting some parts of the biome and altering others (1,2). The results for human health have been profound (1,3).

For practical purposes dealing with maintenance or repair of the biome, the biome can be divided into three distinct parts (Figure 1). One part is ‘host’ in origin, with proteins encoded by human DNA and the products of a multitude of biochemical reactions carried out by those proteins. The remainder of the human biome, all non-human in origin, can be divided into two sub-sets (4). The most widely studied sub-set, the microbiota, contains a wide array of microscopic bacteria, yeast, and viruses. The remainder of the biome, which is often not considered along with the microbiota, is composed of larger intestinal worms (called helminths) as well as some microscopic or near-microscopic protists (often called protozoans).

Disease caused by alterations of human symbionts: the microbiota and recurrent Clostridium difficile colitis
Most alterations in the Westernized microbiota compared to that of our pre-industrial ancestors are due to diet (5–7). Although alterations of the microbiota are associated with a number of chronic inflammatory...
diseases, at the present time there are few established causal relationships between alterations of the microbiota and chronic human disease. A very notable exception to the general lack of proof of causation between changes in the microbiota and chronic disease is the induction of a potentially deadly colitis, which is elicited by destabilization of the gut microbiota following physician-administered antibiotics. This colitis, called *Clostridium difficile* colitis, is the most important cause of healthcare-associated diarrhea (8), although estimating a total number of incidence, for the US or worldwide is difficult because it is not required to report cases (9). Therefore, only rough estimates have been made, and many of those estimates were made 6–10 years ago, at a time when the incidence of *C. difficile* colitis was dramatically increasing. Walters and Zuckerbraun (10) estimated that the incidence in US hospitals increased from 139 000 to 301 200 between 2001–2005, and increased again to 350 000 in 2008, with ~9% mortality each year (11).

The increasing use but decreasing effectiveness of fluoroquinolones are regarded as contributing factors to the sharp increase in *C. difficile* infections (8,9,12,13). The emergence of a particularly virulent fluoroquinolone-resistant strain of the *C. difficile* (*B1/NAP1/027*), which produces increased toxin levels, has been associated with an increase in the incidence and severity of *C. difficile* colitis (14). Further, the high rate of evolution of the bacterium *C. difficile* allows it to adapt quickly to developing circumstances (8,9,12,13), increasing the possibility that problems with recurrent *C. difficile* colitis will only increase in the future. Although estimates vary, the recurrent form, the deadliest form of *C. difficile* colitis, occurs in what is most frequently estimated to be ~20% of the total number of cases (15). The recurrent form of this colitis results when standard pharmaceutical approaches using antibiotics that attack *C. difficile* fail to restore a healthy gut microbiota.

**Resurrecting the microbiota: the case of the fecal microbiota transplant (FMT)**

When understanding the need for policy and regulatory reform, it is helpful to understand the history behind efforts to repair a damaged microbiota by the modern medical establishment. If the microbiota was appreciated as the vital organ that it is, replacement of a lost microbiota and even ‘preservation’ of a microbiota that might be endangered by a medical procedure would have been standard practice decades ago. Certainly the microbiota meets all of the criteria of an organ (16). As with any organ of the body, it can be clearly delineated and has a specific, vital function or functions.

Transplantation has proven an effective treatment for the failure of a variety of organs, and the gut microbiota is no exception. The fecal microbiota transplant (FMT) was first shown to be effective in restoring a healthy gut microbiota and treating recurrent *C. difficile* colitis almost 60 years ago, in 1958, by Ben Eiseman, founding Chief of Surgery at Denver General Hospital, and colleagues (17). Eiseman et al.’s experiments were conducted before it was known that *C. difficile* caused the deadly problem, then known only as pseudomembranous enterocolitis. Even at that time, the problem was on
the rise, and the mortality rates were ‘distressingly high’. In justifying their use of FMTs, Eiseman et al. argued that ‘reintroduction of the bacteria, viruses, and bacteriophage normally found in the colon might re-establish the balance of nature’. They further argued that this process would lead to a decrease in the growth of potentially harmful organisms that had proven, even at that time, resistant to antibiotics. Eiseman et al.’s (17) report in 1958 described four successful fecal microbiota transplants in Colorado, and within a year and a half, a survey of Los Angeles area hospitals showed that 12 patients at seven different hospitals had received a fecal microbiota transplant, with no deaths and 10 of the 12 procedures being successful (18).

Despite the early success of fecal microbiota transplants in resolving an otherwise deadly disease, and despite the easily understood rationale described by Eiseman et al. in the initial report, the procedure remained on the fringes of medical practice. In 1978, C. difficile was identified as a cause of pseudomembranous colitis by microbiologists and surgeons at Birmingham Children’s Hospital (19). The guilty organisms were tested for sensitivity to a panel of antibiotics, but fecal microbiota transplants were not mentioned by the authors of the study. A few reports of fecal microbiota transplants were published during the 1980s through 2005 (15,20), but it was not until 2010 that fecal microbiota transplantation began to gain more attention, with dozens of reports, reviews, and commentaries published since then (21–32). Commonly reported success rates of more than 90% have been typical over the past 10 years, consistent with the initial success rates reported during the 1950s. Despite a history of almost 60 years in Western medicine, fecal microbiota transplants are only now becoming widely accepted, as is evident from the naming of fecal microbiota transplantation as one of the top ten medical innovations for 2014 by the Cleveland Clinic. The recent rise in popularity is not yet complete; people today still die in the US from recurrent C. difficile colitis without ever knowing that a fecal microbiota transplant has a greater than 90% chance of offering them a cure. The question is, why? What are the hurdles preventing the implementation of a cost-effective, life-saving procedure for which there is no effective alternative?

Disease caused by alterations of human symbionts: loss of eukaryotic symbionts

Helminths and protists comprise a component of the human biome that is less well characterized than the microbiota. We and others have argued that the loss of helminths and protists from the human biome in Western society has led to pandemics of inflammation-associated diseases that include essentially all allergic and autoimmune conditions (33,34), and probably include such diverse cognitive issues as migraine headaches, anxiety disorders, and autism (4,35–38). High rates of cancer may also be important in this regard (39,40). At present, these inflammatory disorders reach over half of the US population (41–46).

Pandemics of inflammatory disease resulting from biome depletion are often associated with common environmental triggers and with genetic predisposition, but they do not occur in developing societies, indicating that genetics and triggers are not the cause, per se, of the pandemics. Importantly, many of the molecular mechanisms underpinning the importance of helminths to the human immune system are well understood (47–49). Given the important immune regulation that these organisms provided our ancestors prior to the Industrial Revolution, it would indeed be surprising if inflammatory disease was not a part of our modern, helminth-free society (33).

The return of the complex eukaryotic symbiont: helminthic therapy

Although some helminths and protists are known to cause disease and have been labeled parasites, it is now clear that some exposure to this class of organisms is necessary for human health (3,50). Numerous examples of effective ‘helminthic therapy’ have been found using laboratory animals (48,51,52), and evidence in humans is also quite compelling. The first case of hay fever being resolved following exposure of a human to helminths was reported 40 years ago (53). However, it was not until 2005 that additional studies were conducted, when controlled trials showed that helminths could resolve inflammatory bowel disease in patients who had proven untreatable using modern pharmaceuticals (54,55). Shortly thereafter, a prospective, controlled study in Argentina showed that accidental exposure to a wide range of helminths (the helminths were not intentionally administered) resulted in a halt in the progression of multiple sclerosis (56). In addition, recent socio-medical studies of ‘self-treatment’ practices indicate that the information from published studies is being used effectively outside of mainstream medicine by thousands of self-treaters (35,57). Not only are self-treaters effectively treating inflammatory bowel disease and multiple sclerosis, they are apparently using helminths to effectively treat a wide range of diseases in a manner that was predicted to
be effective by scientists, but that has never been pursued by the biomedical research enterprise. For example, despite predictions by a number of scientists that helminthic therapy might potentially resolve a variety of neuropsychiatric disorders, including depression and anxiety disorders (1,34,37,38), do-it-yourself helminthic therapy practitioners have been the only ones, to date, to pursue the issue in humans, apparently with considerable success (35,57).

**Drugs vs symbionts: fundamental differences**

The primary difference between drugs and critical components of the biome is evident in their respective relationships to human health. Based on current understanding of the human biome, it is absolutely clear that the microbiota is necessary for health. Each individual receives what is essentially an FMT, usually from their mother shortly after birth in a process that is necessary for human life as we know it. Further, it has been argued that the presence of helminths or protists, a fact of life for all humans until recently, is probably also necessary for health (33). With this in mind, an effective and pro-active healthcare system must make available the components of a healthy biome to all individuals of the population for the sake of public health. Just as vitamins are necessary to prevent rickets, scurvy, and beriberi, so is the microbiota necessary to prevent *C. difficile* colitis, and so do helminths or protists likely prevent allergic and autoimmune diseases. Thus, safe and unfettered access to all components of a healthy biome would logically be necessary to maintain health in any society. This view highlights fundamental differences between components of the biome and pharmaceuticals. One is a necessary component for health, and the other is a means of treating disease. The fact that restoration of some component or components of the biome can resolve disease, often more efficiently than any drug, in no way suggests that components of the biome should be considered a drug. No more so than water is considered a drug when it is given to treat dehydration.

The difference between drugs and components of the biome is also evident in their mechanisms of action. For example, the immune modulation afforded by restoring naturally occurring symbionts is fundamentally different than that imposed by pharmaceuticals (Figure 2). The very concept of immunosuppression, the hallmark of pharmaceuticals aimed at immune modulation, is not applicable to therapies aimed at restoration of a biome for the purpose of achieving health (Figure 2).

![Figure 2. Fundamental differences between modulation of immune function by (A) pharmaceuticals and (B) natural components of the ecosystem of the human body. The benefit to cost ratio of pharmaceutical intervention is substantially different than that of biome normalization. These differences should be cause for dramatically different regulatory and policy considerations.](image-url)
saving measures such as vitamin-based therapy, blood transfusions, or kidney transplants.

Mercifully, the FDA used ‘enforcement discretion’ and withdrew their demand for an IND application within weeks of their ‘ton of bricks announcement’. Thus, they paved the way for any medical center to provide FMTs without the requirement for an IND application, and the Centers for Medicare and Medicaid Services (CMS) has approved of the procedure as well as donor screening for insurance coverage. Further, the FDA is committed to not only the safety of the FMT, but also to the availability of the procedure to patients in need.

Even though the FDA and the CMS have now paved the way for any practicing physician to use FMTs covered by insurance for their patients with recurrent C. difficile colitis, the practice is still not standard of care. Thus, the painfully slow pace at which fecal microbiota transplants have been implemented by modern medicine can be attributed only in small part to the action of regulators. Until recently, the medical establishment has been almost entirely uninterested, struggling mightily and somewhat in vain with modern pharmaceuticals to achieve a result that is easily achieved with a transplant. Our biomedical research infrastructure focuses on research involving genetics and molecular pathways and is aimed at the development of chemicals with well characterized mechanisms of action, but it entirely lacks the wherewithal to effectively deal with problems involving simple solutions that involve repairing or restoring a damaged biome. In essence, among all of the agencies, laws, and officials devoted to medicine and public health, not one facilitates or has the power to promote and facilitate the process of recovering a damaged microbiota, despite the fact that the microbiota is well known to be necessary for human health.

The painfully slow 60-year history of incorporating the FMT into modern medical practice is part of a wider problem. The history of the FMT appears to be repeating itself with helminthic therapy. For example, modern medicine has not aggressively pursued helminthic therapy, despite convincing data in animal models as well as controlled studies in humans by Correale et al. (56), now almost a decade old, indicating that the therapy would be highly effective for the treatment of multiple sclerosis. Following up on their original study 7 years later, Correale et al. (60) found multiple sclerosis progressing only in those patients who, because of gastrointestinal distress, had their helminths removed with anti-helminthic drugs. Given that all patients in the study had acquired their helminths accidentally, with no control over either the number or the type of helminth, it is not surprising that some (33%) had intolerable gastrointestinal distress. However, the follow-up study showed convincingly that helminthic therapy using a wide range of helminths is an effective long-term solution for multiple sclerosis. Despite these observations, no patient in the world today diagnosed with multiple sclerosis will be offered helminths by their doctor as a means of long-term treatment. A few patients may be enrolled in a temporary trial where they may receive helminths or a placebo, but even those receiving helminths temporarily will probably receive too few to have therapeutic effect (35). This lack of effective follow-through mirrors that seen during the 1900s with FMTs, and fails to take advantage of an apparently effective and safe approach for which no effective alternative is available at any price.

Pursuit of helminthic therapy has not been completely ignored by modern medicine. In addition to the studies by Correale et al. (56,60) on multiple sclerosis, Weinstock et al. (55) have shown that the porcine whipworm effectively treats inflammatory bowel disease. The porcine whipworm was in the traditional and exorbitantly expensive US drug pipeline for ~10 years before trials were halted due to a lack of effectiveness that has been attributed to an ineffective formulation of the organism (35). What is most disconcerting is not that one particular formulation of one particular helminth failed, but that other formulations are not being aggressively pursued, and that pursuit of one formulation was so expensive. Furthermore, given the dozens of potential organisms which could be used for therapy (61,62), and the dozens of potential formulations that might be used for each organism, it seems likely that a major health initiative with substantial funding is needed in order to effectively, extensively, and rapidly evaluate the potential role of helminths in human health using controlled clinical trials. Certainly such pursuit does not seem forthcoming in the current environment.

Our ongoing work toward regulatory approval for the helminth Hymenolepis diminuta is illustrative of how the present regulatory environment may deal with helminthic therapy. H. diminuta is the second most popular helminth currently used by people self-treating with helminths, and apparently helps resolve a wide range of disease, from allergies to multiple sclerosis to major depression (35). The helminths are maintained in grain beetles, which serve as the helminth’s intermediate host until they are consumed by humans. The production of helminths in this beetle has some advantages to the production of other commonly used helminths, all of which must be isolated from human or porcine feces. Importantly, the beetles are non-toxic: Not only were they commonly encountered by our ancestors without transmitting disease, they are considered a sustainable
food source by the World Health Organization. Further, beetles are already present in our food supply, and this ‘contamination’ is accepted by the FDA. In fact, the level of contamination is only limited by regulation for the purposes of aesthetics: The food is edible but looks unpalatable if there are too many insect parts. A second advantage of raising *H. diminuta* in grain beetles is that tens of thousands of doses of the helminth have been raised and administered to self-treating humans, without reported adverse effects associated with the insect host (35). More importantly, the very common occurrence of *H. diminuta* in the environment (63) with only rare reports of adverse but easily treated side effects (64–69) indicates that the helminths themselves are generally safe. This view of the helminth as generally safe is apparently consistent with the experience of hundreds of individuals self-treating with the helminths (35).

Based on our initial discussions with the FDA, phase II trials (treatment of patients with disease) with *H. diminuta* can proceed essentially in the same manner as Weinstock et al. (55) used the porcine whipworm to treat patients with inflammatory bowel disease. This alleviates time consuming and expensive phase I studies (treatment of healthy subjects) that are an integral part of the traditional pharmaceutical pipeline. If this pattern of moving straight to phase II trials continues, research into helminthic therapy could proceed under the current guidelines at a pace that exceeds the traditional development pathway for pharmaceuticals. If results of eventual phase II trials are as positive as those seen in numerous studies using animal models and in preliminary studies in humans (3,33,35,55,56), we can be hopeful that regulatory agencies will allow the use of helminths in a widespread manner as is currently allowed for FMTs. However, our work towards regulatory approval of *H. diminuta* also reveals some of the flaws of the current system. Before the helminths can be used in human clinical trials, current FDA regulations dictate that the organisms must be purified in a way that dramatically reduces the number of bacteria that may come from the beetle hosts. If this cannot be accomplished, a detailed documentation of the complex ecosystem in the samples must be provided.

Certainly this regulation ensures a minimal number of hypothetical adverse reactions due to impurities carried over from the intermediate host. However, it ignores the demonstrated lack of toxicity of the host organism (described above), and it disregards the fact that purification may actually harm the helminths. Most notably, this regulation ignores the apparent carnage resulting from inflammatory diseases that are due in large part to the absence of the helminths in the human body, as described above. It places barriers in front of the use of the helminths, without weighing the advantages and disadvantages of this barrier. Only the pros are considered, despite the overwhelming disadvantages. To provide some idea of the weighty nature of US regulation, the US is the only country in the world at the time of this writing (April 2016) in which non-infectious helminths cannot be openly shipped as a dietary supplement.

The barriers imposed by regulations explain, in some part, the observation that helminthic therapy has not advanced further than it has, despite its excellent track record. The process places tremendous barriers in the face of any investigator wishing to evaluate the effects of helminthic therapy with *H. diminuta* or any other helminth in their patients. Although *H. diminuta* can be reared at any research institution with modern laboratory animal facilities, it cannot be used in humans in a research setting without first years of work. Not only must investigators apply for grants to fund the necessary research and development to meet largely counterproductive regulatory requirements, they must also complete the research and file a time-consuming application with the regulatory agency. We argue that institutional oversight of controlled exposure to these ancient human symbionts should be sufficient to ensure safety of clinical studies, and, at the same time, facilitate reasonable progress.

At the same time, we wish to make it clear that our attitude is not one of frustration toward the regulatory agency. Indeed, the FDA has been extremely helpful and encouraging as we have moved forward under the current guidelines, however unproductive they may be. Furthermore, as with the FMT, work with helminths seems to be primarily impaired by a lack of interest from biomedical researchers, which is reflected in a lack of peer-reviewed funding for critically needed research.

**Policy and regulations in light of the human as a superorganism**

It is unthinkable that any government organization would devote substantial resources to public health but yet essentially ignore rampant and easily preventable disease due to vitamin deficiency. Such a situation is untenable and overtly irrational. Yet, due to an apparent lack of awareness, an equivalent situation currently exists. The US healthcare infrastructure consumes 10% of the entire GDP but fails to provide the population with vital components of the human biome essential for public health.

Current policy and regulations focus on a surprisingly expensive drug pipeline, with a price tag averaging $2.6
Table 1. Alterations in the human biome caused by modern society.

<table>
<thead>
<tr>
<th>Alterations in the human biome</th>
<th>Causes*</th>
<th>Adverse effects</th>
<th>Call to action**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of beneficial bacteria from the gut</td>
<td>Broad spectrum antibiotics</td>
<td><em>Clostridium difficile</em> associated colitis (70,71)</td>
<td>Formation of agency with authority and resources to pursue FMTs until they are standard of care for recurrent <em>C. difficile</em> colitis</td>
</tr>
<tr>
<td>Alterations in beneficial bacterial flora (5)</td>
<td>For the most part, inflammatory diets</td>
<td>Association with pandemics of immune disease, causal relationship not clear (72)</td>
<td>Focus of policies that promote healthy diets and diet education</td>
</tr>
<tr>
<td>Loss of contact with soil bacteria (2)</td>
<td>Indoor housing, industrialization</td>
<td>Unknown</td>
<td>Policy and resources to encourage soil based probiotics</td>
</tr>
<tr>
<td>Increased contact with pathogenic bacteria and viruses (2)</td>
<td>Urbanization and globalization</td>
<td>Increased triggers for immune disease (2)</td>
<td>Focus on policies that promote hygiene and hygiene education</td>
</tr>
<tr>
<td>Loss of protists and helminths (2)</td>
<td>Toilets, clean water, indoor housing, modern medicine, modern shoes</td>
<td>Pandemics of immune disease (3,33)</td>
<td>Formation of agency with authority and resources to effectively, rapidly, and thoroughly investigate the use of helminths for human health</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Regulate relatively benign helminths as dietary supplements</td>
</tr>
</tbody>
</table>

*With the exception of inflammatory diets (diets rich in fat and processed sugar but low in nutrients and fiber), all causes are necessary components of modern society, with many beneficial effects, not listed here.

**No new regulatory agency is needed, as the FDA is capable of handling everything from the most common food to the most toxic pharmaceuticals. However, a new agency or agency mandate, perhaps part of the NIH or a separate non-profit organization, is needed to promote and advance research and use of FMTs and helminthic therapy.

billion US dollars (2014 estimate by the Tufts Center for the Study of Drug Development). Such costs would understandably present a roadblock for both FMTs and helminthic therapy, which use ‘technology’ that is readily available and potentially difficult to patent. However, at least with the FMT, the FDA and the CMS have proven to be both adaptable and effective at making critically needed therapy available to patients. With what amounts to an assorted collection of convincing phase II clinical trials conducted by a range of medical centers, the FDA has allowed the FMT to be widely used without the burden of the extremely costly phase I through phase III development strategy generally imposed on pharmaceuticals. Further, the CMS has supported coverage by insurance. In essence, the regulatory hurdles that normally face pharmaceuticals have been largely and compassionately swept aside for the FMT. As stated above, it is hoped that regulatory agencies will follow suit with helminthic therapy. However, the problem remains that, regardless of regulatory hurdles, the incredibly slow acceptance of the FMT and the ongoing reluctance by mainstream medicine to thoroughly examine helminthic therapy is a substantial problem. This problem needs special attention by public health officials and by lawmakers.

Policies advancing the use of helminthic therapy may require specific and directed innovation. One possibility is that helminths be regulated essentially as a dietary supplement. Many parallels can be drawn between vitamins and helminths, both of which are necessary for public health as described above, so such regulation is certainly rational. Helminths that are known to cause very few adverse side-effects may work particularly well with this type of regulation. It could be argued that regulation of benign helminths as a supplement will lead to predatory marketing in which ineffective products and exaggerated claims dominate the market. However, current regulations governing the marketing of supplements prohibit unsubstantiated medical claims, and our socio-medical studies (35,57) show that the helminth market which has evolved over the past 10 years is dominated by providers who sell the products they advertise and have well established track records.

The formation of humanitarian organizations to produce and distribute products for biome restoration could be encouraged by public policy, mirroring the collection and distribution of blood and blood products by the Red Cross and Red Crescent Societies. For FMTs, such an organization already exists (OpenBiome) and is currently involved in life-saving production and distribution of material for FMTs. However, the future of the organization could be in doubt if the FDA eventually approves a feces-based product that is shown to work as well as an FMT. It is expected that the FDA will eventually close the window on the humanitarian organization, despite the fact that the humanitarian-based product is likely to be considered the gold standard and will undoubtedly be less expensive than future fecal-based products that make it through the drug pipeline. The production and distribution of helminths or protists by humanitarian organizations is also a feasible approach. Interest in helminthic therapy by the non-profit sector is already evident, with the BioTherapeutics, Education and Research (BTER) Foundation providing research and education on helminthic therapy. However, the Foundation does not
actually produce or distribute helminths. Indeed, current regulations would prevent such activity.

**Conclusions**

The scientific community now widely accepts the view of the human body as a collection of many organisms that exist together in complex, intertwined symbiotic relationships. One component of the human biome, the microbiota, has become a very popular subject of study, and an ever increasing number of scientific publications point toward the role of the biome in health and disease. At the same time, paradoxically, even the most basic information regarding the biome has been extremely slow or even failed entirely to reach clinical application. Some of the apparent reluctance of modern medicine to direct its attention toward repair and maintenance of the human biome can potentially be attributed to burdensome regulations. However, for the most part, the lack of progress appears to reflect little more than a tragic lack of interest from the biomedical research community. In essence, no agency appears to be responsible for applying widely available and vitally important knowledge regarding the role of the human biome in public health.

Just as past policies have placed a barrier in the face of life-saving FMTs, so do current policies place a barrier in the face of helminthic therapy. In contrast, it is hoped that regulations and policy of the future will actively promote restoration of the human biome. It is hoped that regulators and policy-makers will rationally consider and weigh potential risks with potential benefits of biome-restorative therapies, and will actively promote and encourage research and development of biome restoration and maintenance in a way that improves health and decreases healthcare costs. Fortunately, it seems highly likely that other Western countries will do an excellent job with restoration of the human biome, even if the US struggles. Other Western nations already lead the US in both economy and effectiveness of healthcare, suggesting that the approach used outside the US is more rational than the US approach. Wherever successful innovations take place, policy-makers will learn to be proactive rather than reactive, implementing policy and regulations that account for the human being as a superorganism rather than a species isolated from its environment.

**Disclosure statement**

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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