Opening Remarks of the Day 2 session

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This webinar is co-organized by COVID-19 Task Force of the Japan Association for Bioethics to which I belong and the Brazilian Society of Bioethics, which is chaired by Prof. Dirceu Greco. Prof. Greco is highly respected in his research in infectious diseases and bioethics. The title of this webinar is "Pandemic and Research Ethics: Democracy, Placebo, and Post-Trial Access." Today is the second session following last Friday when we discussed mainly on the ethics of placebo-controlled trial. Today's session is more focused on the ethics of post-trial access inviting Prof. Ames Dhai who established the Steve Biko Center for Bioethics, South Africa, and Dr. Tammam Aloudat who has been engaged in Access Campaign of Médecins Sans Frontières (MSF). Prof. Greco, another organizer, will also make a presentation at the last part.

The world situation is drastically changing to overcome this pandemic. As far as we can foresee, something like the global version of United States' Operation Warp Speed might be thoroughly realized now, global supply of effective vaccines collaborating with COVAX. Human rights, justice, and equity play especially important role among the elements of democracy. Today, we wish to listen to the speakers who have contributed to the establishment of democracy in medicine and research ethics. Not only the last week's session, today also, guests from the World Medical Association (WMA), Dr. Otmar Kloiber and Dr. Ramin Parsa-Parsi are participating again. We wish to congratulate the WMA on receiving the prestigious Golden Arrow Award from the Vienna Congress, representing doctors combatting COVID-19 [1]. Prof. Greco, could you please open today's session.

Dirceu Greco
Chair, Brazilian society of Bioethics
Professor Emeritus, Infectious Diseases and Bioethics, Federal University of Minas Gerais, Brazil

It's a pleasure to open this second webinar on this important subject. I am very glad to see all these competent individuals sharing their time to discuss subjects that are very dear to all of us, especially in the situation we are all facing now with the COVID-19 continuous spreading. We need to do so many things about it. This discussion about post-trial access has a lot to do with this ongoing epidemic that unfortunately will not be the last. I pass back the word to the Moderators.

1) Duncan N. WMA Wins Prestigious Award; Otmar Kloiber Acceptance Speech; David Barbe Acceptance Speech. *World Medical Journal*. 2021; 67(1): 11-4.

Kyoko Imamura
Japanese Association of Pharmaceutical Medicine (JAPhMed)/Past President, International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP)
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I am Kyoko Imamura. I am the past president of the IFAPP, International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine, and I am also with Japanese National Member Association, JAPhMed.

Today, I am honored to moderate this seminar, because ethics has been the most important agenda for IFAPP and Prof. Kurihara is the most powerful member of our Ethics Working Group of IFAPP. I found that many of the participants today also attended the last week's session. We have already kicked off and shared most of our concerns and are delighted to have this inspiring discussion.

Today, we are going to have two presentations before we have a short break to go into the second part of our seminar. First, let me invite Prof. Ames Dhai. She is going to touch on the ethics in vaccine allocation in developing countries.

(Published November 15, 2021)

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COVID-19 and bioethics Part 3:
Pandemic and research ethics－Democracy, placebo and post-trial access【Day 2, June 11, 2021】

Ethics in vaccine allocation in developing countries

Ames Dhai [*1]
Professor of Bioethics, University of the Witwatersrand, Johannesburg, South Africa

1. Opening remarks

Good morning, good afternoon, and good evening colleagues. I am Professor Ames Dhai. I established and directed the Steve Biko Centre for Bioethics at the University of Witwatersrand since 2007, and at the end of 2019 retired. I am now Professor of Bioethics and Health Law at the School of Clinical Medicine at Witwatersrand University and Specialist Ethicist in the Office of the President and CEO of the South African Medical Research Council.

I want to thank the organizers of this conference for inviting me to do this presentation today. The topic that I have been given is "Ethics in vaccine allocation in developing countries." I am not going to talk about micro-allocation at individual level or misallocation, but I am going to look at the ethics in macro-allocation decisions for COVID-19 vaccine with particular reference to our developing countries.

2. Presentation outline

By way of outline, I will talk on vaccine nationalism and vaccine equity. I will say a few words on Global Public Good. I will highlight some of the pertinent issues on the African context [1, 2]. I will look at two international documents that call for global vaccine equity and solidarity, which are the Lancet Commission Statement [3] on enhancing global cooperation to end the global COVID-19 pandemic and the UNESCO (United Nations Educational, Scientific and Cultural Organization)'s call in February 2021 [4]. This is its second statement on COVID-19. There is a follow-up one [5] that is being developed, and it is being spearheaded by Prof. Dirceu Greco who is on the panel. I will not discuss that follow-up one and I will leave it to him to bring in if he feels it's necessary.

Subsequently in early May, the world was pleasantly surprised when the United States (US) supported South Africa and India. There was also a flurry of publications on the need for the waiver of the patent. Here

[*1] Founder of the Steve Biko Centre for Bioethics, University of the Witwatersrand, Johannesburg, South Africa; Member and Vice-chair of International Bioethics Committee of United Nations Educational, Scientific and Cultural Organization (UNESCO) (2018-2021)

in this editorial in *Nature*[6], you can see the point is made that a patent waiver is right and fair and wealthier countries must recognize that everyone benefits if vaccine manufacturing is distributed evenly around the world. It also highlights that Africa imports 99% of its vaccines, and African countries lack the preorder purchasing capacity of richer nations. For us to move forward in terms of equitable access to manufacturing vaccines, not only do we have to remove patents, but there has got to be the transfer of knowledge on how to make vaccines and investments in manufacturing capacity.

3. Vaccine equity and vaccine nationalism

When we look at vaccine equity and vaccine nationalism, what exactly are we referring to? It's very simple to understand the issues if we really embrace ethics.

- **Vaccine equity basically affirms human rights.**
- **Vaccine nationalism denies human rights.**
- **Vaccines must be a Global Public Good, accessible and affordable to all.**

Vaccine nationalism degrades the COVID-19 vaccine to a commodity to be sold in the marketplace to the highest bidder. It degrades the COVID-19 vaccine to the bidding and dealing process. This in itself is unconscionable. It's morally reprehensible.

It also erodes the reciprocity and proportionality principles in research ethics by denying those countries from the developing world that participated in the recent trials and contributed to the intervention from accessing the vaccines. Perhaps it is time to push the principle of proportionality whereby if certain countries contributed a certain proportion towards the intervention, then those countries ought to be given first choice for the intervention when available proportional to the contribution made. It's very important when we look at vaccine equity that we must recognize that vaccines must be a Global Public Good and there are many calls for this at international levels, and vaccines must be accessible and affordable to all.

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1) African Union; Africa CDC. Framework for fair, equitable and timely allocation of COVID-19 vaccines in Africa. 31 January 2021.
https://africacdc.org/download/framework-for-fair-equitable-and-timely-allocation-of-covid-19-vaccines-in-africa/

2) Council for Trade-Related Aspects of Intellectual Property Rights. Waiver from certain provisions of the TRIPS Agreement for the prevention, containment and treatment of COVID-19: Communication from India and South Africa. 2 October 2020; IP/C/W/669.
https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=q:/IP/C/W669.pdf&Open=True

3) The Lancet COVID-19 Commission. Enhancing global cooperation to end the COVID-19 pandemic. February 2021.
https://covid19commission.org/enhancing-global-cooperation

4) Joint Statement by the UNESCO International Bioethics Committee (IBC) and the UNESCO World Commission on the Ethics of Scientific Knowledge and Technology (COMEST). UNESCO's ethics commissions' call for global vaccines equity and solidarity joint statement. SHS/BIO/IBC-COMEST/COVID-19 Vaccines. Paris, 24 February 2021.
http://www.sbbioetica.org.br/uploads/repositorio/2021_02_24/Unesco2021GlobalVaccineEquityESolidarityStatement-fev2021.pdf

5) Joint Statement of UNESCO Ethics Commission ensuring equal access for all to vaccines and therapeutic development to confront COVIS-19; Joint statement of the UNESCO International Bioethics Committee (IBC) and UNESCO World Commission for the Ethics of Science and Technology (COMEST). SHS/IBC-COMEST/COVID-19 Vaccines IP Paris, 21 September 2021.
https://unesdoc.unesco.org/ark:/48223/pf0000379042

6) A patent waiver on COVID vaccines is right and fair. *Nature*. 2021 May; 593(7860): 478. doi: 10.1038/d41586-021-01242-1. PMID: 34035532.

4. Understanding Global Public Good

What is a Global Public Good (Table 1)[7]? A Global Public Good impacts spread equitably across the globe without causing division. It is clear in the manner in which the vaccines have been approached that there is a lot of division, and that COVID-19 vaccines as a Global Public Good has not materialized.

A Global Public Good takes into consideration that a price cannot be placed on the benefits of these goods, so the principle of exclusion cannot be applied to it. The use by one individual cannot be allowed to reduce its availability to others. A Global Public Good is not marketable, and the goods and their benefits must be available at negligible or zero cost to all in the global village. We have seen by the many pandemics that we have been having and with COVID-19 which seems to be amongst the worst of all that we are one global village and that a variant can start here today and land up on the other side of the world tomorrow.

Therefore, there are two criteria that determine a public good. It's got to be non-rival in consumption. Consumption by one person must not interfere with the goods being available to others equally. It's got to be non-excludable. Suppliers cannot deny it to those who are unable to pay its market price. Importantly, there are going to be trans-boundary implications with most public goods and in fact there is an ethical imperative for robust international cooperation and action in this context.

5. Cases of vaccine nationalism

Despite the vaccines being a Global Public Good, we saw very early on, in fact soon after the second half of last year (2020), vaccine nationalism and reports and concerns of vaccine nationalism coming through in

Table 1 Understanding Global Public Good

- impacts equitably spread across the globe without causing division.
- price cannot be placed on benefits of these goods:
  - ▷ principle of exclusion cannot be applied to them.
  - ▷ use by one individual cannot be allowed to reduce their availability to others.
- not marketable and the goods and their benefits must be available at negligible or zero cost to all in the global village.
- two criteria that determine a public good:
  - ▷ non-rival in consumption - consumption by one person must not interfere with the goods being available to others equally.
  - ▷ non-excludable - suppliers cannot deny it to those who are unable to pay its market price.
- transboundary implications with most public goods, hence international cooperation and action necessary.

van den Berg RD. Evaluation of the Funding of Global Public Goods Note for the OECD/DAC Evaluation Network – May 27, 2015[7]

7) van den Berg RD. Evaluation of the funding of global public goods-Note for the OECD/DAC Evaluation Network. May 27, 2015. https://www.oecd.org/dac/evaluation/Evaluation-of-Global-Public-Goods-Evalnet-note.pdf

various channels. Amongst the first of these were from Duke University's The Global Health Innovation Center where they published evidence showing that rich countries had gone on a shopping spree for COVID-19 vaccines [8]. This then meant that there would be very few vaccines left for low-income countries.

Many of these countries were going to be able to vaccinate their entire populations several times over again, while low-income countries were at the end of the queue for their turn to purchase vaccines. In fact the data that they put out revealed that several COVAX signatories, including the United Kingdom (UK), the European Union (EU), and Canada were undermining COVAX's pact towards ensuring equitable access of vaccines to all by negotiating side deals with manufacturers for large vaccine shipments resulting in a smaller piece of the pie that would be available to us in the developing world.

6. Countries that have pre-ordered vaccines

Towards the end of last year (2020), the EU was on the top of the list in terms of its preorders followed by US, Japan, and UK, mostly rich countries.

Currently what do we see as of last night? The European Commission orders in terms of the supply agreements on top of the list, but it's good to see that COVAX is catching up, and the African Union has started purchasing as well. It is apparent that while we all see the need for equitable access, if we sit and wait for that equitable access from COVAX, we are never going to get the vaccines. Many of the regions saw it necessary to actually go ahead and get involved in bilateral or multi-lateral agreements.

Currently as of June 9th, we can see the list of countries that have fully vaccinated the share of their populations against COVID-19. These again are mainly the rich countries.

Currently what do we have as of last night again is 17 vaccines that have been approved for use by at least one national regulatory authority. Seven of the vaccines have been authorized by WHO and it is available in its emergency use listing. There are 13.6 billion doses that have been secured globally, and they range in price from $1 to $40. This is clearly highly unaffordable to most of us in the developing world. COVAX has secured 3.86 billion, and it's already shipped 81.9 million doses to 129 countries. Looks good, but it's a drop in the ocean.

7. Who received the first 1 billion vaccines?

Vaccines have developed at a very rapid rate in terms of COVID-19. Already by the end of the April, 1 billion people had been vaccinated only 4 months after the WHO approved a vaccine for emergency use. This was only 16 months after the virus being discovered. Many celebrated this. But, many of us in the developing world looked at such figures, and we said, fine, but who has received the 1 billion vaccines? 75% of these 1 billion went to only 10 countries (Israel: 62.2%, Bhutan: 61.7%, Maldives: 53.4%, United Arab Emirates: 51.4%, United Kingdom: 49.6%, Malta: 48.0%, United States: 41.8%, Chile: 41.6%, Bahrain: 38.8%,

8) Duke Global health Innovation Center. New study shows rich country shopping spree for COVID-19 vaccines could mean fewer vaccinations for billions in low-income countries. November 2, 2020.
https://dukeghic.org/wp-content/uploads/sites/20/2020/11/COVID19-Vax-Press-Release__28Oct2020-1.pdf

Hungary: 37.3%: As of 25 April, 2021, proportion of their populations that have had at least one dose of a COVID-19 vaccine)[9]. You can see in terms of Africa even up to last night, 90% of countries in Africa are going to miss urgent COVID vaccination goals. It's really bad down here.

8. COVID-19 disruptions in Africa and the multilateral approach

Let's consider the ethics of vaccinating people that are not at risk. Vaccinating young adults and moving to vaccinate adolescents while many African healthcare workers have still not received vaccines and many have died is morally reprehensible. Some of us are in the third wave now, so we have concerns of many dying as well. However, high risk populations, those 60 and over have not received the vaccines as yet in Africa while in other parts of the world consideration is being given to and, in some countries, it is being embarked upon to vaccinate the young ones.

The situation of context is, we have had COVID-19 disruptions in Africa (Table 2). You may say, there has been COVID-19 disruptions the world around, but remember, we started off very similar to other developing countries with huge vulnerabilities, huge strains on our health systems, huge economic and social disruptions. These worsened with the pandemic. The gains that we had made on our continent with regard to disease reduction and increase in life expectancy towards reaching our 2030 Sustainable Development Goals (SDGs) have actually gone backwards and that is of concern.

We started off with vulnerabilities, and our vulnerabilities have been heightened by the COVID-19 situation. Early on, our African Union decided to have a multilateral approach to the pandemic response (Fig. 1)[1]. Already in February 2020, it put together the Joint Continental Strategy for COVID-19, and the Africa CDC put together the African Task Force for the Vaccine. The African CDC also together with the African

Table 2 Covid-19 disruptions in Africa

- ▶ Strain on African health systems
  - ▷ PPE shortages
    - ▷ frontline workers ↑ risk → health care workers widespread outbreaks.
    - ▷ Staff shortages.
  - ▷ Disrupted access to non-COVID-19 healthcare services generally.
    - ▷ Disrupted access to essential health services.
    - ▷ infectious disease prevention, routine childhood vaccination, emergency care, and access to life-saving medications.
  - ▷ Disrupted decades of progress - disease reduction and increasing life expectancy.
- ▶ Economic disruptions
  - ▷ socioeconomic status → one of main determinants of health.
- ▶ Social disruptions
  - ▷ Gender, education.
- ▶ ↑ ↑ ↑ ***Vulnerabilities*** *(corruption, displaced persons, refugees, civil war)*

9) Kreier F. 'Unprecedented achievement': who received the first billion COVID vaccinations? *Nature*. 2021 Apr 29. doi: 10.1038/d41586-021-01136-2. Epub ahead of print. PMID: 33927403.

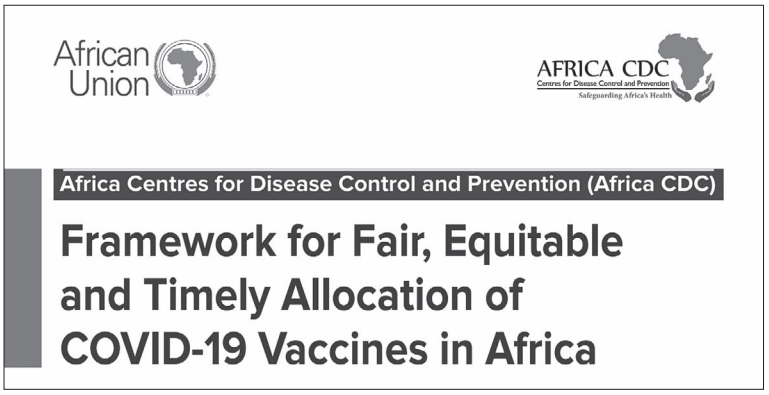
Fig. 1　African Union - multilateral approach to pandemic response

February 2020 – Africa Joint Continental Strategy for COVID-19.

Africa CDC – African Task Force for Coronavirus

Africa CDC – Values Framework

Africa CDC – African Vaccine Deployment Alliance



Source: African Union; Africa CDC. 2021 [1].

Union launched a Values Framework for the Fair, Equitable, and Timely Allocation of COVID-19 Vaccines in Africa.

9. African indigenous values and Umuntu principles

This framework was basically a collaboration between the South African Medical Research Council and the Africa CDC, and it involved a widespread consultation on the African continent. It drew from African indigenous values and Umuntu principles, basically, "***I am because we are, we are therefore I am***" whereby the importance of the community in African indigenous value systems is emphasized and it also emphasized what it means to be a human person (Table 3). We have a saying in Nguni, "***Umuntu Ngumuntu Ngabantu***," "a human being is a human being because of other human beings," and it stresses the inter-dependence and inter-relatedness of humans. We could apply that to the greater good for all while protecting vulnerable individuals and groups.

This would apply both for vaccine access and vaccine hesitancy. We do have a problem with vaccine hesitancy and lack of trust of vaccines, both because of what we have seen at local levels, but also because of us being denied vaccines from the international level. We have an African tradition of lekgotla where all

Table 3　African indigenous values and Ubuntu principles

- "***I am because we are, we are therefore I am***." (Mbiti J): **importance of the community** in African indigenous value systems, and what it means to be a human person.
- "***Umuntu Ngumuntu Ngabantu***" (Nguni saying): a human being is a human being because of other human beings.
  - ▷ **Inter-dependence and inter-relatedness**: greater good for all while protecting vulnerable individuals and groups (for vaccine access and hesitancy).
- African tradition of ***lekgotla*** where all gather under a tree to discuss and exhaust all the options » likened to meaningful **community engagement** in the vaccines discussions.

gather under a tree to discuss and exhaust all options. There are issues to be considered, and we likened this to meaningful community engagement within our vaccine discussions. These are great values and principles. Yes, Africa must take these values seriously and not pay lip service to them. Furthermore, these values could be considered by the world when looking at COVID-19 vaccines as a Global Public Good.

10. Framework for fair, equitable and timely allocation of COVID-19 vaccines

The framework ones drawing from these principles came up with four foundational values:

- **Affirming the humanity of others**
- **Survival of the community**
- **Social solidarity**
- **Meaningful community engagement**

In terms of "**affirming the humanity of others**", allocation decisions must be made such that society at large benefits and the common good is promoted. This could be transposed to the global village where allocation decisions are made such that the global community benefits and common good is promoted throughout the global community.

With "**survival of the communities**", allocation decisions should be based not only the best available evidence, but should look at the greatest risk of severe illness, and other related factors. At a global level, consideration could be given to making allocations to regions with the greatest risk first.

"**Social solidarity**" requires that allocation decisions consider the bonds unifying communities and their interdependence. This could apply to global solidarity when considering the interdependence of countries and our porous borders allowing for ease of movement of variants around the globe.

"**Meaningful community engagement**" will allow for allocation decisions to be trusted. It is such a petty that some of the COVAX donors undermined the COVAX pact such that there emerged distrust of COVAX regarding its ability to deliver in terms of equitable access for all.

11. UNESCO's documents

Article 2 of UNESCO's Statement of the 24th, February this year (2021), stresses that the shortcomings in infrastructure and logistics must be taken into consideration (Table 4) [4]. These shortcomings exacerbate existing divides between the rich and the poor. These shortcomings may restrict the access of the low- and middle-income countries only to certain types of vaccines. It cautions COVAX such that its initiative should not breed discrimination, nor create a situation in which donors would benefit from first-class vaccines and recipients, the lower income countries, receive the second-class vaccines.

UNESCO goes on further to state that for real equity in the global access to vaccines, we need to have a shared ethical recognition of health as a global common good with no territorial limits as well as new global legal instruments for economic and political agreements and treaties (Table 4) [4]. It states that these treaties like the TRIPS were not designed to manage situations like pandemics. It also looks at the issue of the business model of vaccine production. It highlights the responsibility of the pharmaceutical industries to invest in facilities that are able to produce vaccines of the highest possible efficacy, and to facilitate rapid distribu-

Table 4　UNESCO Statement for global vaccines equity and solidarity

2. Ethical concerns for research on vaccines

'Some countries lack adequate infrastructure for such vaccine deployment, which creates an inequality of access, even if the financial bottleneck is resolved through donations. The shortcomings in the infrastructure and logistics needed to ensure equitable vaccine distribution exacerbate the existing divides between the rich and the poor, restricting the access of the low and middle income countries only to certain types of vaccines. The COVID-19 Vaccines Global Access (COVAX) initiative should not breed discrimination, nor create a situation in which donors would benefit from "first-class" vaccines and recipients from "second-class" ones. The unequivocal establishment of efficacy and safety with stringent scientific criteria for all vaccines would alleviate this burden.'

3. Cost, production and distribution: Vaccines as a "global common good"

*'**For real equity in the global access to vaccines**, a shared ethical recognition of health as a **global common good** with no territorial limit is needed, as well as new global legal instruments for economic and political agreements and treaties. The Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) and the agreements of the World Trade Organization (WTO) were not designed to manage situations such as pandemics. ....'*

*'Another issue is the business model of the vaccine production. The IBC and COMEST also underline the **responsibility of pharmaceutical industries** to invest in facilities that are able to produce vaccines of the highest possible efficacy and to facilitate rapid distribution to where they are needed. The massive pre-orders by certain national and regional structures such as the European Union and the African Union demonstrate that health must be treated differently from other markets, and require international economic, scientific and ethical frameworks to regulate investments and returns in this essential field, in a way that does not compromise the wellbeing of the marginalized.'*

(Texts in Italic are quotations from original document. Emphases in bold letters are in original documents, underlined emphases are by author.)

Source: UNESCO 2021 [4].

tion to where they are needed. It emphasizes that health must be treated differently from other markers.

12. The Lancet COVID-19 Commission Statement

The Lancet global commission in February 2021 [3] also highlighted the importance of the TRIPS waiver and urged governments from all regions to agree to the TRIPS waiver as proposed by South Africa and India [2] (Table 5). It went to say that additionally, there needed to be accompanying transfer of technical knowledge for the production and manufacturing of vaccines. It emphasized that this would be in line with the globally agreed target of the Sustainable Development Goal 3.8 which calls for 'access to safe, effective, quality, and affordable essential medicines and vaccines for all.'

Subsequently in early May, the world was pleasantly surprised when the US supported South Africa and India. There was also a flurry of publications on the need for the waiver of the patent. Here in this editorial in *Nature* [6], you can see the point is made that a patent waiver is right and fair and wealthier countries must recognize that everyone benefits if vaccine manufacturing is distributed evenly around the world. It also highlights that Africa imports 99% of its vaccines, and African countries lack the preorder purchasing capac-

Table 5 The Lancet COVID-19 Commission Statement Enhancing Global Cooperation to end the COVID-19 Pandemic. February 2021

'Governments from all regions should agree to implement the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) waiver in relation to prevention, containment, or treatment of COVID-19 for the rapid scale-up of production and distribution of vaccine and therapeutics. Additionally, there must be an accompanying transfer of technological knowledge for production and manufacturing of vaccines. This is in line with the globally agreed target of SDG 3.8, calling for "access to safe, effective, quality, and affordable essential medicines and vaccines for all."'

(Texts in Italic are quotations from original document. Underlined emphases are by author.)

Source: The Lancet COVID-19 Commission. 2021 [3].

ity of richer nations. For us to move forward in terms of equitable access to manufacturing vaccines, not only do we have to remove patents, but there has got to be the transfer of knowledge on how to make vaccines and investments in manufacturing capacity.

13. Conclusion

To confront this tragic moral bankruptcy inherent in vaccine nationalism, what is required is a coordinated global response, which is founded on unity and solidarity. The WHO has said no one is safe until everyone is safe. It's very important to remember that this applies both to within and between countries. Remember, national borders are porous. The right to health and, hence, to COVID-19 vaccine as a Global Public Good applies to everyone in the world and not just to people living in the wealthy high-income countries.

Advancing vaccine availability by sharing of intellectual property, allowing for technology transfer, and supporting local manufacturing of generic vaccines in low- and middle-income countries would go a long way in ensuring that the COVID-19 vaccine is truly a public good and not a commodity to be sold in the marketplace through bidding and dealing. That demand outstrip supply even for countries that have purchased in advance is quite clear. We are seeing that now. Therefore, what is the rational way forward? The rational way forward is that we should ensure that supply is rapidly increased, and this can be achieved if manufacturers and rich countries that back them are prepared to share. Sharing, after all, is caring.

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COVID-19 and bioethics Part 3:
Pandemic and research ethics－Democracy, placebo and post-trial access【Day 2, June 11, 2021】

Médecins Sans Frontières (MSF) Access Campaign for equitable access in the world

Tammam Aloudat
Managing Director, Global Health Center, Graduate Institute of International Development Studies, Geneva, Switzerland

1. Introduction

In terms of introduction, I am a physician, I come from Syria, and I have worked as a humanitarian worker for the past 20 years with the Red Cross and with MSF, the last of which was in the MSF, Doctors Without Borders (Médecins Sans Frontières) Access Campaign for the 3 years.

I have left MSF and started working in the Graduate Institute of International Development Studies as of last week. Currently, I am the Managing Director of the Global Health Center. I mention that particularly because while the experience and the context that I speak from today is acquired through years of working in the humanitarian sector both as a practitioner, as a medic, and a program manager and an advocate in the Access Campaign. I am not representing the official position of the Access Campaign, which is in a way liberating, because I have spent a lot of time since this invitation trying to understand how do the bioethics affect our conception of access from an angle and point of view not of an ethicist but of a practitioner.

2. COVID-19 as a communal outbreak

What I would like to talk about today is the distribution and availability of COVID-19 technologies, that is, as medicines, diagnostics, and vaccines, but within a framework of having worked in multiple outbreaks and with many infectious diseases in the past ranging from cholera to drug-resistant tuberculosis, hepatitis, polio, meningitis, and others.

While COVID-19 is without a doubt a crisis on a very large proportion, it is no less one that shares much of the characteristics of other outbreaks. It stops being only an issue of biomedical disease affecting a patient and becomes a communal, a collective issue that affects larger groups of people. It becomes an issue that engages not only medicine and the medical evidence, but also the politics and the economics and even the values of our communities. The difference here is COVID-19 has done that on a global scale, and rather than having created new conditions, it has emphasized in many cases conditions that have existed before, conditions of inequity, and lack of justice in distribution and position that we have known to exist for a long time but that have largely been hidden from the public view, especially in western settings.

3. Working in low resource settings

The first thing that we are faced with, and I speak as a physician who has worked in low resource settings, is choices. Rather than having the luxury of working in a hospital where someone else allocates resources, and we are told what to treat or not treat, we are put in a position where we have to make decisions about who gets what treatments because of scarcity. Scarcity creates a largely untenable moral position for physicians who are usually not trained for it. I doubt that anyone is positioned in a place where they decide who lives and who doesn't, but that is a place we are put in regularly in very low resource settings and that we have been put in this pandemic on a global setting.

4. Utilitarian versus untenable ethical frameworks

As a practitioner, there are some ethical frameworks that we can try to understand and use. On the face of it, once we start addressing it, it sounds logical except that it starts creating contradictions and this is where we are today. The immediate sort of blanket assumption underneath public health interventions in epidemics or in any high-burden disease settings is that we have a utilitarian ethics where we are trying to use the available resources to provide the most good for most people, except the moment that starts being practiced in reality, the moment it becomes untenable. It's not applicable in a health setting.

I will give you an example. If we were in MSF to provide only the most efficacious and cheapest intervention, we would end up effectively doing a childhood vaccination and nothing else, but we have made different choices including the treatment of a drug-resistant tuberculosis before the last generation of drugs was available at great cost, and the reason is that we cannot think of the situation as static. Treating drug-resistant tuberculosis has pushed the agenda of the disease further. It has made it available. It has allowed us to speak about it, but it also has addressed people who wouldn't have had any recourse otherwise. It is from a clinician's point of view very difficult to adhere to a purely utilitarian ethics. What else?

5. Justice as a principle of medical ethics

One is the one we are provided with that includes the principles of medical ethics include justice in addition to beneficence and non- maleficence. Justice is the odd one out, because it doesn't talk about the relationship exclusively of a clinician or a patient. It talks about the position of medicine in society and talks about distribution. However, it's never been put to a test at this scale at least in such a public forum, and this is important, because it does not talk about biomedicine only. It doesn't talk about need purely. The need is intersected by economics and by politics, by the position of people in their countries, the position in their class, the position in their gender, and so on.

Then we are faced with situations where we are both put in a position of responsibility vis-a-vis the health of people that are under our care and have been stripped off much of the authority that remains in the hands of sovereign states that on their own have other interests that compete with those of providing best healthcare. This is obvious if we look at some of the statistics. The comical addressing of, for example, the United

States (U.S.) health system whereby the expenditure is nearly double the next country and their position in terms of life expectancy or other health indicators is down in the 20s and 30s. The interest in providing the most efficacious healthcare to the largest number of population is not absolute and is not practiced equally.

6. TRIPS waiver and vaccine distribution inequality

We end up being put in a position where there is an extreme inequality in distribution of whatever available resources and in our case here the one obvious case is the vaccine. We end up having to choose what sort of action constitutes the most ethical one under the circumstances. MSF and many others have rightly chosen to address the issue of WTO (World Trade Organization)-TRIPS (Agreement on Trade-Related Aspects of Intellectual Property Rights) waiver. TRIPS waiver has a merit of addressing an instrument of international norm that restricts access and has a potential to be quite restrictive to the distribution of vaccines. This is a population that has softened as Prof. Ames Dhai mentioned who would have thought that the U.S. administration of all would be one that supports the waiver.

What that means in practice is difficult to anticipate, because it's not only about waiving the intellectual property. It is also about sharing knowledge, about sharing technology, about accepting that we cannot accept an automatic intellectual property on products that have been developed by public funding. It addresses the whole system and the waiver if anything is treatment of a symptom. It is treatment of a symptom of a symptom. As we all know, treating symptoms might be necessary, but it never solves the problem entirely. By that I mean the waiver treats one of the symptoms of intellectual property regime that we are forced to accept, but the intellectual property regime itself along with the imbalance of research and development and the allocation of resources, in themselves symptoms of a world we find ourselves in that accepts the commodification of medicines and hence the commodification of people that live in it except the sovereignty of states as a higher value than the health of people and so on. We are in a situation where we are contented or forced to contend with treating the symptoms of a symptom than the waiver and addressing the consequences of a trade regime that accepts profit on medicines and on people's habit is the one viable route we have.

7. Issues outside of vaccines waiver

But what I will go for now is for the next few minutes try to address some of the issues that we have faced that were outside the immediate vicinity of the waiver and the vaccines that have come up in different context in the lifespan of this pandemic. One of them is the access to healthcare and our ability to accept massive degrees of inequality among different populations and here the availability of healthcare itself. It's no secret the healthcare in North America and Western Europe and as well as other rich countries like Japan, Australia, and New Zealand and so on is by default at an entirely different level than many other poorer countries. Yet we have allowed a course of discussion in the first months of this pandemic to focus on the availability or unavailability of ventilators when we had ventilators necessary to address 2% to 5% of patients in the early stages of the pandemic.

Most of the debate about the management of this pandemic before the vaccines became available or were known to be coming has focused on whether the 2% to 5% of the population in richer countries are going to have optimal care. Not that this is negligible. This is important and this is a massive dilemma, because in the

early stages in Italy, the Association of Anesthetists, for example, issued guidelines about how to take people off ventilators if they had less chances of survival to put people who might survive better. That in itself has implications that are unimaginable to most practitioners in normal times, to take someone off of ventilator and let them effectively perish so someone else can benefit from the same machine.

While at the same time, very little mention was done to the fact that let alone that there aren't ventilators in most of the world, there isn't passive oxygen in most of the world. There aren't ICU beds; there aren't ICU doctors or nurses. That was rarely on the TV except when it was trivialized and characterized like when someone said, "But the Hall of X country in Sub-Saharan Africa has only two ventilators and one of them is booked, is reserved for the President's family." This in itself we could talk about condescending and trivializing discourse rather than argue about why would the country have two ventilators in this day and age. It was made almost a quasi-joke to be put on TV.

That extends to the continuation of that dismissive discourse about countries including Africa doesn't have any cases. The Middle East doesn't have. We don't see them. This is a disease that has affected Europe and the U.S. beyond anyone else, while fully knowing that there are no diagnostics and there are no effective registration systems that would give us a real image. We have contended ourselves with dismissing. It went as far as publications that asked what do we need to learn from Africa and why did they not have – well, they did. The fact that we don't see it doesn't mean it doesn't exist. In my own experience despite the lack of numbers, in my country in Syria, there has been a wave of COVID that has largely unreported because it couldn't be diagnosed, but suddenly you start hearing about relatives who are older who die vaguely from diseases that never affected them that severely before. COVID has ravaged through the rest of the world, but we have managed to dismiss it.

8. Access to medicines and diagnostics

The next one is the access to medicines having suffered this wave of information and misinformation and different evaluation of information, but then also the access to diagnostics. The fact that we have ended up with diagnostic tools that are old. At least the PCR diagnostics aren't ones that are new technologies. The PCRs and machines and cultures have existed before, and we have used them to diagnose drug-resistant tuberculosis among other things. Suddenly, their availability became abundant after years and years of trying to make some of them available for other diseases and this is another contextual issue. We are all proud with how science progressed and made available diagnostic tools and vaccines within months and ignore that same could probably have happened for other diseases and that it didn't.

9. Two regimes of global health

Here I will go back to 10 years to a significant article in my opinion by Andrew Lakoff who talks about two regimes of global health [1]. He talks about a regime of global health that is the global health security that

1) Lakoff A. Two regimes of global health. Humanity: An International Journal of Human Rights, Humanitarianism, and Development. 2010: 1(1): 59-79. DOI: 10.1353/hum.2010.0001

addresses largely diseases that haven't existed yet and aims largely at the protection of western countries, rich countries, from the potential of new diseases. Here the response is aggressive, generous, and rapid. Then there is another global health regime which he calls humanitarian biomedicine, which addresses diseases that are familiar, cheap to address, and yet not addressed like drug-resistant tuberculosis, like neglected tropical disease, leishmaniosis, sleeping sickness, and so on and so on that have needed decades of scarce resources to develop any sort of technologies. In fact, sleeping sickness which still exists in many pockets in South Sudan, Nigeria, Congo, and others didn't get a new diagnostic and treatment until they were developed by non-profit entities like DND*i*, Drugs for Neglected Diseases *Initiative*, which has developed the first non-injectable treatment for sleeping sickness ever.

10. Vaccines as excludable and rivalrous good

Finally, the vaccines. Here is an interesting point, because as Prof. Dhai said, very early in the process there was this talk about vaccines being a global public good. Now there is a point that Prof. Dhai mentioned which is the same countries that proclaimed it a Global Public Good turned away almost instantaneously and started buying vaccines, hoarding vaccines, and we know the statistics, the countries that bought 500% or 300% of what they might need just to guarantee that they will have it early enough.

But the view of Global Public Good as a non-excludable and non-rivalrous, vaccines are excludable and rivalrous. If someone takes a vaccine, someone is not going to take that vaccine. Vaccines are not like clean air or clean water. They have a cost to produce, and when they get consumed, they disappear. It begs the question about whether that has served only as a sort of a sloganistic way of making everybody feel good while the richer countries manage to occupy the market and hoard almost every vaccine where we see the consequences now with nearly full coverage. The United Kingdom yesterday was discussing whether 12 years old at nearly no risks should be vaccinated. It's almost completely justifiable in most western media that this would be a legitimate discussion before healthcare providers have been vaccinated almost anywhere else.

11. Governance for global health

Then, we are left in a place where governance for global health is scattered between sovereign states that are increasingly protective and look inwardly and frames that are put outside as unchallengeable and impossible to change like the fact that medicines and vaccines and diagnostics have to be treated as commodities that go through a market despite all the imperfections and failures of that market which needs public funding and needs IPs to protect, but yet, we are offered no alternative and not allowed to think of any alternative.

A few days ago I read a definition of governance, because supposedly we work on global health governance, but as you all well know, the literature still contests the definition of what global health is and what governance is, so it's a bit difficult, but sociology book from the 60s argues that governance is making people want to do what is needed and failing that making them do what is needed. Governance includes a coercion part implicit to it. There is no requirement of governance to be only democratic or only benevolence, and the problem here is not only making people want to do something but to do what is needed. The decision on what

is needed and what is the global health is taken by a very narrow strata of managerial class, and by philanthropic capitalists and billionaires, and by civil servants who owe their loyalty to their next elections before the health of the people and the rest of the world. That governance, if we do not think that it has left much to be desired under the current pandemic, then we need to reconsider what we think of as success or failure.

12. Global health crisis

This is particularly interesting not only because newer pandemic will come. I have worked in 2005 in Indonesia when the H5N1 was going to be the next pandemic and then in 2009 when actually H5N1 was a pandemic. We have seen Severe Acute Respiratory Syndrome (SARS) happen; we have seen the Middle East Respiratory Syndrome (MARS) happen. We knew a pandemic is going to come, and arguably we haven't been prepared, but not only that we are in a global health crisis that has global implications and yet rather than becoming an equalizer as we were promised in the beginning, it has become another reason for deepening the inequalities that are affecting the people, the inequalities as a result of the COVID itself, but then the others that we haven't yet started exploring that include all the other mortality and morbidity that has happened and is happening in the background and is ignored now, because everybody is paying attention, all the unnecessary child and maternal and infectious disease and non-communicable disease deaths that you have even less access to healthcare.

13. Conclusion

From a position where we as practitioners have to function in this system and still be able to go and have a good night's sleep, hopefully some of the nights at least, there is a difficulty in accepting that there are many days where we have to actually deal with the symptoms of the symptoms. We have to go and pretend the TRIPS waiver will solve everything, and there are days where that stops being enough. I wonder whether we could have an argument one day about an ethical decision that accepts the basis of global health being vertical, run by the west, continues legacies of power and inequality, and owes its allegiances to member states rather than people.

We might need to answer those questions faster than we think because now we are dealing with a single virus with a single potentially vaccine to deal with it and we are struggling to find a solution. In 20 years, we will deal with climate crisis that will make many other diseases differently endemic, we will have no single vaccine to deal with it, and probably be much more expensive and create much more inequality.

I thank you very much for having me because this is a place where we can hear the ethicist guide us. I have very much in my career benefited from listening to people tell us how to think better about the ethics of our practice.

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Discussion (Day 2 No. 1)

Chieko Kurihara
Specially-appointed Professor, Kanagawa Dental University, Japan

Thank you very much Prof. Ames Dhai, Dr. Tammam Aloudat for the very valuable talk about equitable access of many kinds of resources not only vaccine. We Japanese have to recognize shameful government attitude to buy top vaccines for the nation despite the low prevalence comparing Brazil and many other countries like African and European countries. First of all, I would like to invite Dr. Peter Lurie, because he cannot stay until the end. His Citizen's Group is very much engaged in challenging to overcome this kind of inequity in the world.

Peter Lurie
Center for Science in the Public Interest, Washington, DC, the United States

It's very, very difficult to say anything that can add much, certainly not to top what we have just heard from our previous speakers, extraordinarily well put together, beautifully stated, eloquent, and unfortunately mostly unheeded, really a beautiful set of comments. I want to thank you for that.

I only have a couple of things to add because so much has already been said. On a personal note what I found so frustrating about all of this is that this so-called end or ending of the pandemic is exactly the ending that many of us saw coming down the tracks one year ago. This seemed like a virus that was maybe unusually susceptible to vaccination compared to, say, HIV. It seemed that the concerted attention of the scientific establishments around the world would be able to produce something, and indeed within a relatively short period of time it has. But it was equally predictable or perhaps even more so that we would wind up in a situation in which some people who had only limited need for the vaccine would wind up with it and those who clearly would need it would wind up without. That was exactly the situation that was predictable a year ago. It's exactly the situation in which we find ourselves today.

It speaks poorly of humanity as a whole that with all of this concerted attention of almost literally every person around the world knowing about this pandemic going on that we have somehow failed to come up with a solution that is much better than what we have had in the past.

Yes, there have been some signs of progress in COVAX and the recent announcement just yesterday by the Biden Administration of another 500 million doses. Yes, those things are admirable, the endorsement of the TRIPS waiver by the U.S. is also helpful, but at the end of the day, we find ourselves where we usually do, which is with the haves having and have-nots not having. It is just exasperating to see the same play taking place repeatedly.

The second thing is I am not an official ethicist the way some of the people on this call are, but I have taken part in a number of these debates over the years. Sometimes these debates are theoretical. They are about principle. But this one is not merely about that. This is a debate in which literally life and death is at stake,

what we should call a global misallocation of vaccines, a public health malpractice has taken place, and the price is not paid in principle, but it is paid in lives, likely in the hundreds of thousands, probably in the millions. All of these tiny little debates, say, in the United States on whether vaccination should be for 65 year olds or 60 year olds or whether frontline worker should go before healthcare workers are so trivial in comparison to this global misallocation of resources that it's just extraordinary. This is the big debate. This is the true injustice of this epidemic, and it's the same one we have seen taking place for years.

The final thing I will just say is here in the United States, we focus on our so-called newspaper of record which is the New York Times, and it's done a pretty wonderful job of covering this pandemic with a lot of personal stories, very well-done statistical analyses that have run every single day, a section that was devoted to the pandemic running 7-8 pages every single day, and on the weekend a special social piece called "At Home." Just this past week, the New York Times decided to do away with those sections. I am not here to say that that's wrong from a journalistic point of view. At some point, you can't cover a story forever, but I believe that in some western countries, the perception is growing that somehow this pandemic is ending. It's just not so.

In some countries, a number have been mentioned in the Middle East, for example, this pandemic is just beginning. The self-satisfaction of the people in the West about the accomplishments of science, the occasional gestures in favor of vaccine availability just do not take that into account. I suppose that all paths forward begin with a conversation, and I suppose that this is one of them. Let us hope that when the next pandemic comes, because it surely will, we will do better than we did this time.

Ruth Macklin

Distinguished University Professor Emerita at Albert Einstein College of Medicine in New York City, the United States

I want to thank both speakers for their excellent presentations. I started formulating my brief comment and question before I heard Dr. Aloudat's, but now I have to add him to it, because of his seconding and very interesting and thoughtful remarks.

I am in total agreement with the points that both speakers have made. Prof. Dhai's presentation understandably focused on the role of governments and nation states in a global pandemic, including references to international documents and UNESCO. My question, and Dr. Aloudat briefly touched on the issue: what about the private sector? Big pharma in this world stands to make billions and billions in profits. They have already made billions from profits in many other contexts. The next big one coming along is the recent scandal of the U.S. FDA (Food and Drug Administration) having approved a drug for treating Alzheimer's disease that researchers found not to be efficacious. There is lots of money the drug company can make, given all the aging people who already have Alzheimer's and those likely to acquire it in the near future.

Big pharma is a player as a vaccine producer. There is no way to coerce big players in private industry anymore then there is to coerce nation states. But why not call for wealthy, profitable industries--not only pharma, but especially pharma--to contribute to the needs of LMICs (Low- and Middle-income countries) in the COVID pandemic?

Tammam Aloudat

Managing Director, Global Health Center, Graduate Institute of International Development Studies, Geneva, Switzerland

In the same spirit of pragmatism, we cannot wait until every problem is solved, because people's lives are on the scale. One thing is how do we deal with today? There are things that have been informed about and talked about absolutely clearly from the beginning including how can we give billions and billions of dollars and Euros as subsidies to pharmaceutical companies without demanding of them anything but vague promises of access?

In the global south that has meant unaffordable prices because they get to set the prices, but even in the global north this meant that the taxpayers are paying the price twice. They have paid them in subsidies to the pharmaceutical companies and then they are paying them again in prices of vaccines. It's hard for me to conceive, and I don't come from a democracy, but when you are in the democracy, how do those things come to pass and what sort of dogma allows this to be normal? But that's beside the point. There can be conditionality on public money. Their protectionism in the name of we can't sacrifice the economy for the pandemic is too thin to hold that long. That didn't happen, but there were very good cause and the governments should be held accountable for the billions they expended on subsidizing pharmaceutical companies without demanding solid and clear returns in terms of access conditionalities.

The second question for the future at least in my view is, we like market or not, capitalism or not, is it viable for the world to put our collective health and survival in the hands of CEOs whose primary goal is to increase shareholder profitability? Is that a sustainable way to go forward? That is a significant question. I have an opinion that none is probably interested in, but this is a debate that has to be had. We can't just sacrilege the profit and the market to the extent that whoever dies and then we end up with the argument on whether Boris Johnson did say, "let the bodies pile higher", or he didn't exactly say it. Doesn't matter if he did or he didn't, because every other government acted as if they are saying it when they have given almost freehand to the market over the health of their own people.

Ramin Parsa-Parsi

Workgroup Chair of the 2013 revision of the Declaration of Helsinki

German Medical Association

Thank you again Prof. Kurihara for inviting me to participate in this important meeting. This was an interesting and very good and rewarding experience. I would also like to thank our two speakers today, Prof. Dhai and Dr. Aloudat. I appreciated your presentations and agree with you that lifting or waiving patents of vaccines is not enough. It doesn't suffice. We also need a knowledge transfer for vaccine manufacturing. This is probably even more important. That's an opinion I would absolutely share.

I took a lot of notes during the two meetings, especially getting back to our thoughts around the Declaration of Helsinki [1)] and the CIOMS guidelines [2)] and tying back into the discussions we had during the first part of

1) World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research involving Human Subjects. Adopted Jun 1964, last amended in Oct 2013.
https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

2) Council for International Organizations of Medical Sciences. International Ethical Guidelines for Health-related Research Involving Humans. 2016.
https://cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/

the event. Prof. Macklin highlighted the differences between the CIOMS and Declaration of Helsinki guidelines with regard to this specific paragraph on post-trial access. Prof. Kurihara, we also took note of your proposal that communities should probably also be included in this process, not just the individual trial participants. Post-trial access is a matter of extreme importance and has to be considered before research begins.

The issue of community engagement before the beginning of a trial should be discussed. This should involve all the different stakeholders, meaning sponsors, big pharma industry, developers, investigators, the trial subjects, but also governments. It should involve all these parties in order to get to a fair and good outcome and to ensure the success of the trial, also after it has been completed. This is all something we will need to confer about and discuss again once we revisit the documents focused on clinical trials. I am referring here primarily to the WMA (World Medical Association) Declaration of Helsinki (DoH) because that's the document that will most likely be reviewed again soon. It was helpful to have the differences between the DoH and the CIOMS guidelines highlighted again. The meeting provided valuable feedback which we will certainly consider, and I will also forward this feedback to the WMA Medical Ethics Committee for consideration.

I took a lot of good thoughts from these discussions. Thank you.

Ames Dhai

Professor of Bioethics, University of the Witwatersrand, Johannesburg, South Africa

Thank you so much for the comments, Dr. Parsa-Parsi and Prof. Macklin. To go back to Prof. Macklin in terms of big pharma not being given emphasis, the Article 3 of the UNESCO document [3] that I presented does emphasize the need to look at that business model. There has to be change to that business model. It also emphasizes the responsibilities of pharma that have to materialize meaningfully into action as well. Yes, while presenting a general overview, pharma was included into the discussions. You can't leave out big pharma in terms of the culprits they are as well. What we have seen with the vaccines, more especially vaccine nationalism and the bilateral agreements is that there are concerns all round to include high income countries, their governments, and pharma. Perhaps it's time for countries' governments in the developing world to say to big pharma, we are not going to allow you to do any clinical trial here unless there is that promise or that undertaking that we will have access to the interventions, not only for those that were involved in the study, but also to our populations that participated in some way or the other, and this needs to come from our government levels so we need commitment at that level as well.

Kurihara There are many things to discuss. Especially we have to collaborate with pharmaceutical companies, and we wish to change the previous policy of companies after experiencing of this COVID-19 situation.

(Published November 15, 2021)

3) Joint Statement by the UNESCO International Bioethics Committee (IBC) and the UNESCO World Commission on the Ethics of Scientific Knowledge and Technology (COMEST). UNESCO's ethics commissions' call for global vaccines equity and solidarity joint statement. SHS/BIO/IBC-COMEST/COVID-19 Vaccines. Paris, 24 February 2021.
http://www.sbbioetica.org.br/uploads/repositorio/2021_02_24/Unesco2021GlobalVaccineEquityESolidarityStatement-fev2021.pdf

COVID-19 and bioethics Part 3:
Pandemic and research ethics－Democracy, placebo and post-trial access【Day 2, June 11, 2021】

Post-Trial Access for All: Perspective of achieving universal access to adequate public health*1

Dirceu Greco*2
Professor Emeritus, Infectious Diseases and Bioethics, Federal University of Minas Gerais, Brazil

1. Opening remarks

Let me start by thanking again the Japanese partners of this very interesting seminar, Japan Association for Bioethics. The Brazilian Society of Bioethics is proud to be with you, and this event is very important for all of us.

What I am going to talk now is a continuation of what Prof. Ames Dhai said very well and what Prof. Ruth Macklin last week and Dr. Peter Lurie spoke about today. We are facing just a tip of an iceberg that affects us all, but I am going to try to make it clear when I start talking. First of all I have no conflict of interest to be declared in this presentation.

2. Two hypotheses

I have some hypothesis (Table 1).

Research has to be relevant with social value. We need to have international ethical guidelines to be followed. In clinical trials, access to proven preventive, diagnostic, and therapeutics must be provided without

*1 Previous lectures and papers on related topics published in *Clinical Evaluation* can be seen from the following, especially the reference No. 1:
- Presidential Symposium in the 40th Annual Scientific Meeting of the Japanese Society of Clinical Pharmacology and Therapeutics, 2019 International Collaborative Research and New Trends of Research Ethics /
The 120th Pharmaceutical Study Group Meeting Ethics of international collaborative research: Perspectives from Brazil
http://cont.o.oo7.jp/48_1/48_1contents_e.html
- COVID-19 and bioethics: Part1 Ethical Challenges and COVID-19
The Recommendation No. 01/2020 of the Brazilian Society of Bioethics (SBB)
http://cont.o.oo7.jp/48_3/p661-84.pdf

*2 Chair of the Brazilian Society of Bioethics, 2019-2021; Member and Vice-chair of International Bioethics Committee of United Nations Educational, Scientific and Cultural Organization, 2018-2021

1) Greco D. Shimoda K, Watanabe H, Organizers. The Past, Present, and Future of Ethics of International Health Research: Research as a stepping-stone to Universal Public Health Care Access. *Clin Eval.* 2020; 48(1): W29-W53.
http://cont.o.oo7.jp/48_1/w29-w53.pdf

Table 1 Hypothesis

- Research with human subjects must be relevant, with social value.
- International ethical guidelines for research are also necessary.
- In clinical trials access to best proven preventive, diagnostic and therapeutic must be provided, without double standards, including post-trial.
- Results of human research must be translated into public health access.
- Access is even more important and urgent in public health emergencies – e.g., patent exemption for COVID-19 products must be issued.

Hypothesis 2: Access post-trial as a right

The obligation to guarantee post-trial access to products (and care) if these are shown to be effective (and safe) is based on the following ethical principles:

- The principle of beneficence requires that the welfare of participants be actively promoted.
- The principle of non-maleficence requires that the welfare of participants is not negatively affected due to the interruption of non-access to efficacious products.
- The principle of justice:

As **reciprocity** calls for providing something in return to participants who have volunteered their time, been inconvenienced or experienced discomfort by enrolling in the trial.

And also as **distributive justice**, a notion pertinent to situations that call for the fair allocation of benefits.

double standards including post-trial. Results of human research must be translated into public health access. That is going to be my motto today. Access is even more important, not exclusively, and urgent in public health emergencies, for example, patent exemption for COVID-19 products must be issued.

My second hypothesis is access post-trial as a right (Table 1). I argue that obligation to post-trial access to products and care is based on many ethical principles; "beneficence" requires that the welfare of the participants be actively promoted, "non-maleficence" requires that the welfare of participants is not negatively affected due to the interruptions or non-access to efficacious products, and maybe the most important is the principle of "justice", being "reciprocity" as part of it and more importantly "distributive justice" as a notion pertinent to situation that call for fair allocation of benefits.

These are two hypotheses I am going to detail now.

3. What is owed following a clinical trial?

I was trying not to make so much about discussing the post-trial access after trials, as my main point, and I am going to put myself forward as a physician, an infectious disease expert. I have been dealing directly with the effects of pandemics. I have been very much involved with at least two of them. The first one was HIV-AIDS that hit all of us and still hitting the whole world and now COVID-19. My emphasis is much more in the public health system than on the usually very controlled clinical trial. And I am going to show you what some selected documents have established. Prof. Ruth Macklin mentioned some of them.

I will start with CIOMS 2016 [2], one in relation to clinical trials. It's on Guideline 1, Guideline 2, and Guideline 6.

UNESCO [3, 4] has a lot of items and they were already mentioned by Prof. Ames Dhai. One of them is Sharing of Benefits, Article 15.

The 2007 UNAIDS/WHO Guidance document [5] that Prof. Macklin and I participated very strongly on its establishment, but which unfortunately, has been succeeded by a very much lax document which was just released [6].

The 2010 WHO Guidance on Ethics of Tuberculosis [7] is a very good document, and it addresses a lot about public health access.

The 2013 Declaration of Helsinki [8] Paragraph 34 on post-trial access is lax in this subject.

I am going to talk a little bit about a developing country position imbedded in the 2012 Brazilian Research Ethics Commission, resolutions 404 and 466 [9], on post-trial access.

My argument is that the right to post-trial access in a clinical trial is a dated discussion, because the main focus of all of us should be to ensure access to the benefits of trials in public health to all, not only in the COVID-19 pandemic.

4. CIOMS 2016 – Guideline 2 and Guideline 6

The CIOMS 2016 [2] Guideline 2 is bit lax about post-trial access, because it says that "***as part of their obligation, sponsors, and researchers must also***" and I don't like this following wording "***make every effort***". It doesn't mean anything to say "***...in cooperation***", "***to make available...***". To make ***every effort*** and ***to make available***, it is not very clear what we are saying about post-trial access. That is the first point.

Guideline 2 does not specifically mention post-trial access, but in Commentary of Guideline 6, it says, "***As***

2) Council for International Organizations of Medical Sciences. International Ethical Guidelines for Health-related Research Involving Humans. 2016.
https://cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/

3) United Nations Educational, Scientific and Cultural Organization. Universal Declaration on Bioethics and Human Rights. 19 October 2005.
https://en.unesco.org/themes/ethics-science-and-technology/bioethics-and-human-rights

4) Joint Statement by the UNESCO International Bioethics Committee (IBC) and the UNESCO World Commission on the Ethics of Scientific Knowledge and Technology (COMEST). UNESCO's ethics commissions' call for global vaccines equity and solidarity joint statement. SHS/BIO/IBC-COMEST/COVID-19 Vaccines. Paris, 24 February 2021.
http://www.sbbioetica.org.br/uploads/repositorio/2021_02_24/Unesco2021GlobalVaccineEquityESolidarityStatement-fev2021.pdf

5) Joint United Nations Programme on HIV/AIDS (UNAIDS) 2007. Ethical considerations in biomedical HIV prevention trials: UNAIDS/WHO guidance document. 2007.
http://data.unaids.org/pub/manual/2007/jc1349_ethics_2_11_07_en.pdf

6) Joint United Nations Programme on HIV/AIDS and World Health Organization; 2021. Ethical considerations in HIV prevention trials. Geneva; 2021. Licence: CC BY-NC-SA 3.0 IGO.
https://www.unaids.org/sites/default/files/media_asset/ethical-considerations-hiv-prevention-trials_en.pdf

7) World Health Organization. Guidance on ethics of tuberculosis prevention, care and control. 2010.
https://apps.who.int/iris/bitstream/handle/10665/44452/9789241500531_eng.pdf;jsessionid=A807FA85616DD9B062232400AD281696?sequence=1

8) World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research involving Human Subjects. Adopted Jun 1964, last amended in Oct 2013.
https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

9) Brazilian Research Ethics Commission Resolution 466/2012, which succeeded Resolution 404/2008.

part of their obligation to transition to care after research, researchers and sponsors may have," again the verbs employed all the time are not "must", nor "have to", but it is "may have", and "make every effort". This is not a strong position related to post-trial access.

On the other hand, CIOMS 2016 Guideline 1 may be understood as an added protection for post-trial access, because it says and that is the strongest stance that they make: that "***Scientific and social value cannot legitimate subjecting study participants or host communities to mistreatment or injustice.***" We must keep an eye on this, specifically on avoiding ***injustice***.

The CIOMS Guideline 6, but again I am not going to go through all this very busy slide. In commentary, it states again, "***may have to provide continued access to interventions***", but also that sponsors and researchers may no longer have an obligation to provide continued access to a study intervention that has demonstrated benefit when it becomes available in the public health system. Worse than that, it says that "***sponsors, researchers, and community members may agree before a trial starts that any intervention that has demonstrated significant benefit will be provided for a predetermined period of time***". It makes everything very easy to make a case for not providing exactly what people believe are going to get.

5. UNESCO 2005 Universal Declaration on Bioethics and Human Rights

UNESCO 2005 document [3] is a document I consider very important as it was approved by 1996 countries, but it still lax in relation to post-trial access, because it says, in the item Sharing of benefits: "***Benefits resulting from any scientific research and its applications should be shared with society as a whole and within the international community, in particular with developing countries***." That's very good, but unfortunately, it says that "***benefits may take <u>any</u>*** (Emphasis by underline is added by author. The same applies hereinafter.) ***of the following forms***". "*Any*" of course means "any of them". One of them is very good: "(c)***provision of new diagnostic and therapeutic modalities of products stemming from research***" and "***(e)access to scientific and technological knowledge***". But if may interpret the possibilities in different ways, you may choose one, two or three of mentioned forms. You may, for instance, chose *capacity building* or *support for health service*. My opinion is it should include all (and not any) of the listed possibilities or at least that some of them must be always included. In my opinion, one of these should be "***provision of new diagnostic and therapeutic modalities of products stemming from research***".

6. Ethical considerations in biomedical HIV prevention trials 2007 - UNAIDS/WHO guidance document

The UNAIDS/WHO 2007 document [5], unfortunately, this has been succeeded by a revised one [6]. This is an important document, because it speaks very strongly for benefits for people that are participating, and in the end, it says that "***some of the activities related to the conduct of biomedical HIV prevention trials which <u>may</u> benefit those who participate <u>may</u> actually be rights***". That's a good point, but I consider that instead of "may" it should be "must". This document has been updated in 2021 [6] but in my opinion the new position on this point is weaker than in the 2007 Guidance Document.

7. Declaration of Helsinki: Post-trial access

We now come to Declaration of Helsinki [8] and I have very many criticisms (Table 2). I have spoken about that many times. In 2000, I participated in the approval of important changes in the Declaration (Edinburgh, United Kingdom). In 2008, I was also in Seoul, South Korea, for another revision of the Declaration. I did not manage to participate in the General Assembly that approved the current version (Fortaleza, Brazil). It is worth emphasizing that in 2000, for the first time, the right to post-trial access was very clear: "***Every patient entering a study should be assured of access to the best proven prophylactic, diagnostic, and therapeutic methods identified by the study***".

This was changed in 2008 and again in 2013. Now it says that "***in advance of a clinical trial***", those people "***should make provisions for post-trial access for all participants who still need an intervention identified as beneficial***"; "***This information must also be disclosed***." The difference you see here, "should make provisions" in the 2013 version is very different from "should be assured". This is weaker than in the 2000 version, and there was a fierce discussion on the subject between 2000 and 2013. I hope that the WMA (World Medical Association) after considering all arguments in favor of the right to post-trial access, and especially with what's happening with COVID, may consider again a stronger language for the coming version, basing in then Declaration of the 2000 version.

8. WHO 2010 – Guidance on ethics of TB prevention, care and control

This is a very important document. It's from 2010 and again from WHO [7]. It's on ethics of tuberculosis

Table 2　The WMA Declaration of Helsinki: Post-trial access

Edinburg 2000
30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.
Seoul 2008
33. At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.
Fortaleza 2013
34. In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.

prevention, care, and control, and it's very strong in the defense of participants and also on access in public health (Table 3). Prof. Dhai mentioned when should we permit trials to be done in our countries. This Guidance provides a list of sine qua non prerequisites for permitting a clinical trial. I wish to highlight two circumstances in which biomedical trials should not be performed: "***When agreements have not been reached among all research stakeholders on access to medical care and treatment***"; and "***when agreements have not been reached on responsibilities and plans to make trial products (drugs, other treatments, or preventive measures) that prove to be safe and effective, available to communities and countries where they have been tested, at an affordable price***." Although this is a WHO document I think it is not followed as it should.

This Guidance goes on and detail the rights to access to TB care for all, and the obligations to provide TB services. They use questions to elaborate on: "***Do governments have an ethical obligation to provide universal access to TB care?***" "***Yes***". Many important documents are mentioned such as WHO Constitution and

Table 3 WHO 2010 Guidance on ethics of TB prevention, care and control: Access to care for all

WHO 2010
Guidance on ethics of TB prevention, care and control
Access to care for all

Does this obligation mean that tb care should be provided for free?

- **Yes.** "Anti-TB drugs should be available free of charge to all TB patients, both because many patients are poor and may find them difficult to afford, and because treatment has benefits that extend to society as a whole (cure prevents transmission to others)" - *Stop TB Strategy*

Considerations are particularly important in designing an ethical research strategy.

- Research should be designed so that the populations in which it is carried out stand to benefit from the results.
- Research results should lead to **technology transfer**, whenever applicable, for the benefit of the affected population.
- Research protocols should provide attention to how findings will be translated into public health policy, as applicable.

2. The obligation to provide access to TB services

Do governments have an ethical obligation to provide universal access to tb care?
Yes. Provision of universal access to TB care is grounded in their duty to fulfill the human right to health.

As stated in **the WHO Constitution,** "the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition".

Similarly, the **International Covenant on Economic, Social and Cultural Rights** recognizes "the right of everyone to the enjoyment of the highest attainable standard of physical and mental health" and specifically calls on State Parties to take steps necessary for "the prevention, treatment and control of epidemic, endemic, occupational and other diseases".

(emphasis added)

Source: WHO 2010 [7]. Table is reproduced from *Clin Eval*. 48(1) [1].

the International Covenant on Economic, Social, and Cultural Rights from UN, and in these it is based the argument that universal access to the TB care is grounded in their duty to fulfill the human right to health. It can be applied also to the COVID-19 pandemic.

In the same document, another question: does this "obligation" means that TB care should be provided for free? Yes. That is specific for anti-TB drugs, but why not for other drugs, for other diseases that are also prevalent throughout the world. I want to elaborate on this. The COVID-19 pandemic came not as a substitution for the other problems that we have. It's an add-on. If it disappears, we are going to have a lot of things to take care of and I hope we can another three, four, five meetings like this to discuss how to tackle them.

The document mentions that research results should lead to technology transfer. That's exactly what I have been saying about COVID-19, and the research protocol must provide attention to how findings will be translated into public health policies. What we have been discussing in South Africa, Brazil, in many other developing countries, and undeveloped countries especially in relation to the waiving of patents is part of the solution. It has been difficult because of the pressure from the big pharma, the money that is involved, which makes it very hard for people to counteract. But we must be part of this counteracting.

9. Brazilian Research Ethics Guideline

I am going to tell you a developing country position regarding research ethics. This is a case study that I consider is very interesting, and it is about the Brazilian Research Ethics Guidelines and the Unified Health System, which has as its acronym SUS (*Sistema Único de Saúde* -Unified Health System). SUS in Brazil is completely public, financed by taxpayer's money, and provides access to health to all 210 million Brazilians. I am going to remember just one specific date, that is 1st of August 2008, and this is just two months before the 59th WMA General Assembly that changed the 2000 Declaration of Helsinki.

Brazilian anticipated the results of this GA especially in two specific items. First, Brazil was proposing to cancel the two notes of clarification approved by the WMA, related to flexibilization on the use of placebo and on post-trial access. Those weakened the rights of the volunteers, and the Brazilian Health Council approved Resolution 404/2008 [9] keeping what was stated in the 2000 version of the Declaration of Helsinki. I am not going to read the terms of Res. 404 which are in this slide, but will call you attention especially in relation to access to healthcare: it says that participants at the conclusion of the study will be provided with the best proven prophylactic, diagnostic, and therapeutic methods identified by the study.

It is worth emphasizing, and everyone knows, the Declaration of Helsinki is not binding. It's a very good document, very important, very respected, but the countries, if they can make it even more strict, the better. That's exactly what Brazil did at that time. In this resolution, it was also included the proposition to further discussion on access to health and to the products that have showed efficacy, not only in a clinical trial, but to all who need them, in public health.

Of course, these points were later embedded in the newer resolution 466/2012, that succeeded the original research ethics guidelines (res. 196/96) (Table 4). It explicitly defines that at the end of the study, the sponsor must ensure to all participants access free of charge and for all the needed time the best prophylactic, diagnostic, and therapeutic methods identified by the study. And it goes on stating that there is no time limit. If it shows to be safe and effective, it must be provided, independently of the products getting to the public health

Table 4 Brazilian Research Ethics Commission Resolution 466/2012*

III.2 – Research involving human beings in any area of knowledge must: ensure to the participants adequate conditions of follow up, treatment, access to new drugs (if shown to be safe and effective)
III.3 – In biomedical research:
d) At the end of the study the sponsors must ensure to all participants, access, free of charge and for all needed time, to the best prophylactic, diagnostic and treatment that have demonstrated to be efficacious
d.1) Access will also be warranted between the end of individual participation and the end of the study. In this specific situation access will be permitted through a study extension, according to a consubstantiated analysis of the participant's attending physician.

**** Succeeded Resolution 404/2008 (1 August 2008), which also included:***
To propose further discussion on access to health and to the products that have showed efficacy to all who need them.

(emphasis added)
Table is reproduced from *Clin Eval*. 48(1) [1].

system or not.

Brazil is, to my knowledge, the only country with such a strict and protective position. When this resolution was issued, many people said that big pharma would not do research in Brazil anymore. But this has not happened. What actually happened is that they adapt their clinical trials to the Brazilian Guidelines. This may be explained, at least partially, because for them the drug market in Brazil is one of the largest in the world. Thus, if they have to give up a tiny part of their enormous profits, they will still make a lot of money. Thus, the Brazilian example could be used by many other countries, but this has not happened... And of course, big pharma continues to pressure the Brazilian authorities to make these two items more flexible.

10. Brazil's Universal Public Health System (SUS)

The Universal Public Health System is of paramount importance, because that is what we expect globally. Dr. Lurie or someone else has mentioned that the public health system in the United States is amazingly bad and exclude many people from care. Brazil, a country with an enormous disparity, which makes me ashamed, has public health system that includes everybody - 210 million people can have access to it. The exemplary response to the AIDS epidemic, providing care and antiretrovirals free-of-charge to all, is a good case study and it happened only because we have this system. Of course, the system is under-financed and has been overwhelmed now by the COVID-19 pandemic, but the appalling situation with the current pandemic would be even worse without the SUS. It is worth noting that although everyone has the right to access the public health system, less than a 4th of the population also have private insurance.

We can give an idea of the magnitude of the public health system in Brazil in terms of numbers. Its dimension is really amazing. It has the world's largest human milk bank. Organ transplantation is also one of the world's largest. It funds 90% of preventive vaccines, 80% of treatments in oncology. All antiretroviral drugs and the still very expensive antiviral drugs (for hepatitis C) are exclusively funded by the system. I must emphasize that everything is funded exclusively by municipal, state, and federal taxes. All this is in danger

to be lost with the neo-liberal/right wing policies in place in Brazil today.

As mentioned before, it is a successful example. I will show a summary of what Brazil put in place to confront HIV/AIDS. This is 2009, but it is very similar in 2020: Brazil has the same HIV prevalence as in North America and Europe, that is, 0.4% for the general population, and this was due in part by the issuing in 1996 of a law giving the right to all people living with HIV/AIDS to receive the needed antiretroviral treatment. And in Brazil has available 21 antiretrovirals to everyone who needs it and close to half of them by local public laboratories. This is a very interesting example that if there is political will and ample participation of the whole society, things can be done even in situations of disparity as we have in this country. And of note, just once, Brazil issued a compulsory license for one drug (efavirenz) from Merck. The price decreased from $1.45 per tablet to $0.6 and it is produced in Brazil since then. The next slide gives an idea of the magnitude of the public health system in Brazil in terms of numbers at is just an example, a sample.

11. COVID-19 pandemic in Brazil

As you all know, Brazil is a big country. I live in Belo Horizonte, which roughly 400 km inland, both from Rio and San Paulo and we are almost 20,000 km away from Japan! But what I wanted to show you is that as of June 2021 Brazil has 17 million cases of COVID-19, with an unacceptable death toll (biweekly deaths per million was 77, compared to 1.36 in Japan, as of middle October) almost 500,000 people who have died from COVID-19 and these numbers could be a lot lower if irresponsible federal government had acted sooner. But they have negated the seriousness of the epidemic. It took them a long time to decide to buy vaccines, to join the COVAX Initiative and to establish proper nonpharmacological preventive measures, such as use of masks and social distancing. As Dr. Lurie mentioned, a few countries are saying that in very little time they are going to have epidemic under control, but that will certainly not happen anytime soon globally. What is happening now is some industrializes/developed countries which have most of the world's wealth are buying most of the COVID-19 vaccines available. Currently Brazil has only 14.6% of the population fully vaccinated, even producing two of the vaccines locally. And will follow discussing the need for expanding worldwide production of patent-free vaccines and other products for COVID.

12. WTO (World Trade Organization)

The Brazilian SUS is shown again as it is an important tool to guarantee sustainability. This is about HIV, but it is very similar to COVID and other infectious diseases. There is a need for technology transfer. We may start using the flexibilities allowed by WTO (World Trade Organization) - TRIPS Agreement (Agreement on Trade-Related Aspects of Intellectual Property Rights) defined by the WTO Doha Declaration. However, it is not enough to use the Doha Declaration on TRIPS. As mentioned above, Brazil just once used a compulsory license [10], but now we are in another situation that relates to post-trial access for all, globally. This slide

10) Greco D, Invited lecturer. Kimura R, Special guest. Victoria Perottino M, Guest Discussant. Saio T, Kurihara C, Organizers & Discussants. Ethics of international collaborative research: Perspectives from Brazil: Part 1 Selected notes on Paulo Freire: Part 2 Access, Compulsory license, Case Study. *Clin Eval*. 2020; 48(1): W95-W123.
http://cont.o.oo7.jp/48_1/w95-w123.pdf

shows the approval of TRIPS Agreement in 1995 and also the following Doha Declaration, but even if it is possible to use Doha Declaration for compulsory licensing, it is almost impossible to do that in an urgent situation and globally, not only because of red-tapping, but also the difficulty to use all the tools and knowledge that is needed to the actual producing of needed products: vaccines, drugs, other devices. Big pharma usually does not open all needed knowledge for the production of these goods.

Thus, it was really a good thing that in 2020 South Africa and India spearheaded a proposal to the WTO to waive product patents to control COVID-19 globally. These two countries belong to the BRICS (Brazil, Russia, India, China, South Africa). Unfortunately, Brazil in the beginning did not join them. Recently in part due to the United States decision to back this proposal, the Brazilian government agreed only to participate in the discussion of the proposal. South Africa and India's initial proposal, now backed up by over 130 countries, was very comprehensive, that is they ask for the temporary suspension of several provisions, including copyright, industrial designs, patents, and undisclosed information. With that, it will be feasible to many countries that have well-prepared, well-equipped laboratories and researchers, to start producing very soon. It is worth emphasizing that over 10 countries are qualified by WHO to produce human vaccines. The other thing that should be worth fighting for after or concomitantly with the discussion of this temporary suspension, is a revision of the TRIPS Agreement itself which today impedes the access to many other needed products for other illnesses. It is really just that intellectual property rights should be equally applied both for consumer goods and health products? I don't think it should, so maybe if the waiver is approved it could be a good start.

If the waiver is applied for COVID-19 products, this could also happen post-pandemic for all diseases that affect many people worldwide. In Brazil, several health, Bioethics institutions have backed the WTO proposal: a statement was issued in February 2021 by the Brazilian Society of Bioethics, the Brazilian Association of Collective Health, the Brazilian Center of Health Studies and United Network supporting the not patenting of products developed to confront COVID-19 [11]. In addition to the document issued in February, 2021 [4], as Prof. Dhai mentioned another document on the need for international solidarity in relation to access to vaccines for all is to be approved by UNESCO [12]. There is a lot of discussion on this issue. A new draft is being discussed as a joint statement by UNESCO's ethics committees (IBC and COMEST) with the objective of ensuring equal access of vaccines for all and agreeing with the proposal to suspend patents of vaccines and related products developed to confront COVID-19. It is not still consensual among the committees' members (approved after this webinar). I hope it will become consensual, because with so many people, so many individuals, so many governments, backing that up, UNESCO should be in the same boat in this situation.

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11) Position of the Brazilian Society of Bioethics (SBB), the Brazilian Association of Collective Health (ABRASCO), the Brazilian Center for Health Studies (CEBES) and the United Network (Rede Unida) for the not patenting of products developed to confront COVID-19. February 27th, 2021.
http://www.sbbioetica.org.br/uploads/repositorio/2021_03_24/SBBEEntidades-on-Patents-10Mar21-english1.pdf

12) Joint Statement of UNESCO Ethics Commission ensuring equal access for all to vaccines and therapeutic development to confront COVIS-19; Joint statement of the UNESCO International Bioethics Committee (IBC) and UNESCO World Commission for the Ethics of Science and Technology (COMEST). SHS/IBC-COMEST/COVID-19 Vaccines IP Paris, 21 September 2021.
https://unesdoc.unesco.org/ark:/48223/pf0000379042
(Approved after this webinar.)

13. Conclusion

I always liked this 1964 quote from Norberto Bobbio, an Italian philosopher. He said that "***the greatest problems of our time in relation to the human rights, is not any more to set its foundations but to protect them***". What is it saying is that we have everything in our hands to do what we need to do. When we say we, I am being a bit too immodest, because there are many hurdles, but the tools are there. We must make pressures so that the available tools can be used throughout the world, especially in situations that we are seeing in many diseases.

The first conclusion is that is true that we need better preventative methods, more efficacious and less expensive drugs and many more efficacious vaccines. Clinical trials with these objectives can be performed where vulnerability is lower. We are arguing that if it proves effective, it has to be distributed throughout the world. All stakeholders should participate in all the stages of the study, from the developing to the application, and it's crucial to develop universally acceptable ethical principles. If ethical standards are lowered, it will certainly be difficult to eventually raise them. This is the kind of criticism to what happens with some of the documents that I mentioned before - some of them were very strict and protective, and now they are laxer, maybe wrongly adapting according to the new times and the prevailing neoliberalism.

Decisions about post-trial access should be based on the principles of justice. Volunteers must have access to drugs, vaccines, prevention strategies, and any other study benefits. In my opinion, the discussion on access to care and treatment in research may be considered dated. The endless debates about the rights of participants to post-trial access must be substituted with a broader and more difficult objective of providing access to all efficacious products of research in public health. It is not my phrase, the next one, but I want to emphasize that the *status quo* of inequality must not be an immutable fact and that we must fight for universal access to health, which must be truly recognized as a human right and not as an economic commodity.

Just to remind you all, what I said in the beginning, I am repeating in the end, is that COVID is not just one but more epidemics we have to face. If you look at diseases listed here, at least 20 of them are included among what is called Neglected Tropical Diseases (https://www.who.int/teams/control-of-neglected-tropical-diseases/overview). I agree with many that they should be called diseases that disproportionally affect neglected populations. It is more appropriate to consider like that, because many of these diseases we have in Brazil, but I am not affected by them, because I am not part of the neglected population. Three other diseases are not included in this list, AIDS, Tuberculosis, and Syphilis, because there are specific programs to tackle them. In 2013, the World Health Assembly adopted a Resolution calling for a world decision to prevent, control, eliminate and eradicate these diseases. In 2015, they released a new document with a kind of roadmap for this end. As mentioned before there are many documents, and there are tools to be used to eliminate, to prevent or to control most of these diseases. I add that there is money to do it, but unfortunately there is the need to have political will, plus our participation as concerned citizens, together with civil society to demand actions to make it clear that these diseases must be controlled.

I am going to conclude with two quotes and a tribute. I hope it applies to us here: Thucydides writing on the Peloponesian War mentioned that "***Justice will prevail when those who are not subjected to injustice are as indignant as those who are***." I may be considered as part of this indignant group, because I'm not directly

subject to injustice: I am a physician, I am white, I can work and I have a salary, but of course I am an exception compared to most people in the world. On the other hand, I dare to say that "***justice will prevail when those affected by injustice are able or emancipate themselves to fight for their rights***". Of course, we should take part in fighting for that. In Portuguese, many people use "empowerment" for Thucydides quote. I prefer to use emancipation instead of empowering people. This is a sense frequently used by the late Brazilian educator Paulo Freire. People can be empowered, but I understand that we cannot empower people as people can emancipate themselves.

One more quote is from Cuban Jose Marti when he says that "***my country is humanity***". Maybe that's a way that we now together in this international discussion may also consider. If everyone is not saved, no one will be saved. And my tribute is to London 2012 Summer Olympics in their opening ceremony. They honored the United Kingdom National Health System, and the people that were part of this opening ceremony were NHS (National Health System) nurses. That's a very interesting and direct way of saying that it is essential to have a national health system. And very recently, during the COVID-19 pandemic, an airplane from a company from United Kingdom had this phrase on its fuselage, "Thank you very much National Health System." I finish now saying again, thank you to all of you.

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COVID-19 and bioethics Part 3:
Pandemic and research ethics－Democracy, placebo and post-trial access【Day 2, June 11, 2021】

Learnings for ethics from Covid-19

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1. Learnings from Covid-19 and our past approaches to ethics in research

Since the beginnings of bioethics as a discipline in the 1950's, perhaps nothing has challenged the international ethics community more than the present Covid-19 pandemic. Where did our rights-based ethics find itself within the science, politics, and economics of biomedical research during this global public health crisis? As a community of ethicists were we sufficiently prepared to address the urgency of medical research and public health measures during a time when we were perhaps most needed? Did we resolutely and in solidarity with one another critically evaluate our own role in health-related research and the structures of ethics in our international organizations, national frameworks, and institutional practices? Were we as ethicists and members of this international teachers' and researchers' community in ethics sufficiently self-critical? To these questions, unfortunately, we must respond emphatically, No.

Ethics has enjoyed a long presence in the debates on what is morally acceptable in biomedical research based largely on widely influential international guidances going back to the *Nuremburg Code* (1947)[1)], the *Declaration of Helsinki* (1964-2013)[2)], the CIOMS *International Ethical Guidelines for Health-related Research Involving Humans* (1982-2016)[3)], the UNAIDS *Ethical Considerations in HIV Preventive Vaccine Research* (2000)[4)], the WHO *Operational Guidelines for Ethics Committees Reviewing Biomedical Research* (2000)[5)], and the WHO *Handbook on Good Clinical Practice* (2005)[6)]. We have, however, failed during this

1) Nuremburg_code.pdf. (n.d.). Retrieved 8 February 2021.
https://www.fhi360.org/sites/all/libraries/webpages/fhi-retc2/Resources/nuremburg_code.pdf.
2) World Medical Association. Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. 2013. (n.d.-a). Retrieved 8 February 2021.
https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
3) Council for International Organizations of Medical Sciences. International ethical guidelines for health-related research involving humans. 2016.
https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf
4) UNAIDS. Ethical Considerations in HIV Preventive Vaccine Research: A UNAIDS Guidance Document. 2000.
https://data.unaids.org/publications/irc-pub01/jc072-ethicalcons_en.pdf
5) World Health Organization. Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participant. 2011.
https://apps.who.int/iris/bitstream/handle/10665/44783/9789241502948_eng.pdf?sequence=1&isAllowed=y
6) World Health Organization. Effective Media Communication during Public Health Emergencies: WHO handbook and field guide. 2005.
https://www.who.int/csr/resources/publications/WHO_CDS_2005_31/en/

most critical time for individuals, communities, and public health generally to provide a critical reflection on the way medicines are being developed and public health measures are taken.

2. The Covid-19 challenge

Already in September 2020, the Secretary General of the United Nations, António Guterres warned us:

> The pandemic is a clear test of international cooperation — a test we have essentially failed . . . . [due to] a lack of global preparedness, cooperation, unity and solidarity [7].

Early in the pandemic the international community promised to share its learnings, to share the evidence of the findings of its research, to share the data, and to share the fruits of the research that was driven by public funding. Now in June 2021, as already in September 2020, the international community, as well as those responsible inside nations, failed to measure up to the needs for solidarity in a global health crisis. Rather, as Secretary General Guterres pointed out, and tried to warn us, we have been utterly failing in our preparedness, cooperation, and sharing of scientific and economic resources during this pandemic. No amount of tinkering with international guidelines can make up for this failure. Ethics needs to recognize (not undermine) the central place of human dignity in biomedical research while providing a critical response to human experimentation and public health measures that undercut the fundamental values sought for informed consent, ethics review, and respect for persons.

Covid-19 has been identified in nearly all countries. There are currently 173 million reported cases and 3.73 million deaths worldwide (as of June 2021). We have seen an enormous impact from this virus on health: physical health, emotional health, psychological health, and (outwardly) economic health. The response from ethics to Covid-19 research and public health measures has been lacking. We have excluded people, we have excluded voices, and we have downplayed the work that was critical. We have entered into our own silos, and we have gone back to what is comfortable with regards to ethics and with regard to the discussions that we have had in ethics rather than to move forward and look at the situation as it is today, not the situation when with UNAIDS began this discussion in 1997 or when the World Medial Association picked it up in1999 and 2000 or it was later followed by CIOMS. This cannot be strictly an historical discussion on who said what when and where. We can say looking back over the course of this discussion on placebo-controlled trials and post-trial access to the “best-proven” intervention that we have failed to place ethics, and to prepare ethics, for playing a significant role in health-related research. The failure has been extraordinary.

3. Placebos and post-trial access to medicines during Covid-19

During this pandemic, a number of ethicists have again confronted the discussion on the role of placebos in clinical trials on medicines addressing Covid-19 [8] as well as the question of post-trial access to medicines by individuals and populations [9]. As in the past, standard of care and the rights of trial participants and their

7) United Nations. Secretary-General Highlights ‘Essential’ Failure of International Cooperation, in Address to Security Council Meeting on Post-Coronavirus Global Governance. 24 Sep 2020.
https://www.un.org/press/en/2020/sc14312.doc.htm

communities absorb the focus of this discussion. Fair questions. However, the inability of the ethics community to come to terms with what is at stake in placebo-controlled clinical trials and post-trial access to medicines, including in regions where they have had less familiarity, may lie in a certain intransience in posing the question:

> The dominant bioethical position . . . . ensured that inequalities of power and resources were perpetuated, not remedied, by the AZT debates [10].

Since the early 1980's azidothymidine (AZT) had been studied in clinical trials using placebos in patients infected with the human immunodeficiency virus (HIV) and experiencing the resulting acquired immunodeficiency syndrome (AIDS). While the AZT trials raised safety concerns, the drug was shown to have significant efficacy [11]. The United States Food and Drug Administration (FDA) approved AZT for AIDS Related Complex (ARC) in March 1987 [12].

In response to concerns raised by ethicists and scientists regarding the use of AZT in these placebo-controlled studies, the US NIH issued the following statement:

> It is an unfortunate fact that the current standard of perinatal care for the HIV-infected pregnant women in the sites of the studies does not include any HIV prophylactic intervention at all. Nor does the standard of care for these HIV-infected women include the combination therapies recommended and used for some HIV-infected women in the U.S. However, the inclusion of this regrettable, but real, performance-site standard in the form of placebo controls provides the direct comparison of standard and new intervention that is needed to form the basis for rational policy decisions and will result in the most rapid, accurate, and reliable answer to the question of the value of the intervention being studied compared to the local standard of care [13].

In 1997, Marcie Angell (then Editor of the *New England Journal of Medicine*), published a highly cited editorial [14] questioning "the placebo-controlled trial orthodoxy" and the apparent "slavish adherence to the

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8) Ortiz-Millán G. Placebo-controlled trials of Covid-19 vaccines - Are they still ethical? *Indian J Med Ethics*. 2021 Apr-Jun; VI(2): 1-8. doi: 10.20529/IJME.2021.015. PMID: 33908358.

9) Moodley, Keymanthri, and Theresa Rossouw. South African COVID-19 vaccine trials hold key lessons for future partnerships. The Conversation. 9 Feb 2021.
https://theconversation.com/south-african-covid-19-vaccine-trials-hold-key-lessons-for-future-partnerships-154676

10) Wendland, Claire L. "Research, Therapy, and Bioethical Hegemony: The Controversy over Perinatal AZT Trials in Africa." African Studies Review, vol. 51, no. 3, Cambridge University Press, 2008, pp. 1-23.
http://www.jstor.org/stable/27667377.

11) Fischl MA, Richman DD, Grieco MH, Gottlieb MS, Volberding PA, Laskin OL, Leedom JM, Groopman JE, Mildvan D, Schooley RT, et al. The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. A double-blind, placebo-controlled trial. *N Engl J Med*. 1987 Jul 23; 317(4): 185-91. doi: 10.1056/NEJM198707233170401. PMID: 3299089.

12) Brook I. Approval of Zidovudine (AZT) for Acquired Immunodeficiency Syndrome: A Challenge to the Medical and Pharmaceutical Communities. *JAMA*. 1987; 258(11): 1517. doi:10.1001/jama.1987.03400110099035.

13) The Conduct of Clinical Trials of Maternal-Infant Transmission of HIV Supported by the United States Department of Health in Developing Countries: A Summary of the Needs of Developing Countries, the Scientific Applications, and the Ethical Considerations Assessed by the National Institutes of Health and the Centers for Disease Control and Prevention 1994-1997. July 1997.
http://www.columbia.edu/cu/musher/AIDS_case/nimh_cdc_review.htm

14) Angell M. The ethics of clinical research in the Third World. *N Engl J Med*. 1997 Sep 18; 337(12): 847-9. doi: 10.1056/NEJM199709183371209. PMID: 9295243.

tenets of clinical trials" in the context of AZT trials carried out in Côte d'Ivoire, Uganda, Tanzania, South Africa, Malawi, Thailand, Ethiopia, Burkina Faso, Zimbabwe, Kenya, and the Dominican Republic. She considered that up to 16 studies funded by the US Centers for Disease Control (CDC) and National Institutes of Health (NIH) as well as by UNAIDS, 15 of which involved the use of placebos against AZT. Nevertheless, her editorial board supported the publication of such trials in "the *Journal*" (prophylaxis vs placebo study against tuberculosis in the same issue of the *NEJM*) after having cited the Declaration of Helsinki, which clarifies the requirements that "the goals of the research are always secondary to the well-being of the participants."

Now in the midst of a crisis of public health, science, and ethics during this Covid-19 pandemic, in stark contrast to the Declaration of Helsinki, bioethicists from the National Institutes of Health in the United States argued that the obligations researchers have

> . . . to their participants are distinct from the obligations that clinicians have to their patients . . . . The differences between the ethics of clinical research and clinical care are reflected in the consensus that it can be ethically appropriate to invite research participants to accept some risks to collect socially valuable data [15].

These government ethicists, however, provide no references to their assertion of a "consensus" that individuals should take risks for "socially valuable data." They argue that – based on urgency, informed consent, and ethics review – placebo-controlled studies for the Pfizer and Moderna Covid-19 vaccines, even after they have been shown to be 95% and 94.5% effective:

> [Others] argue . . . that researchers conducting clinical trials are obligated to treat participants consistent with their clinical interests and conclude that it is unethical to give participants a placebo once a safe and efficacious vaccine has been identified. We disagree. This view fails to recognize that the obligations researchers have to their participants are distinct from the obligations that clinicians have to their patients.

When researchers, who are also clinicians, fail to consider the obligations we have toward their patients' health as patients (even when they are also research participants) in favor of some perceived urgency, contribution to their perceived needs of science, the public good, or "data," then we have returned to the kind of government research of the 1950's and 1960's where ethics was essentially consider "for others, not for us" [16].

A near same position was then taken by the WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation [17], who also argued that placebo-controlled trials were justified:

> [We] believe it is ethically appropriate to continue blinded follow-up of placebo recipients in existing trials and to randomly assign new participants to vaccine or placebo. Moreover, under these conditions, we believe that trial sponsors are not ethically obligated to unblind treatment assign-

15) Wendler D, Ochoa J, Millum J, Grady C, Taylor HA. COVID-19 vaccine trial ethics once we have efficacious vaccines. *Science*. 2020 Dec 11;370(6522):1277-1279. doi: 10.1126/science.abf5084. Epub 2020 Dec 3. PMID: 33273060.

16) Baker R. The human radiation experiments: final report of the President's Advisory Committee on Human Radiation Experiments. *Med Hist*. 1997;41(2):256-257.
https://www.osti.gov/opennet/servlets/purl/129478/129478.pdf

17) WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation, Krause PR, Fleming TR, Longini IM, Peto R, Beral V, Bhargava B, Cravioto A, Cramer JP, Ellenberg SS, Figueroa JP, Halloran E, Henao-Restrepo AM, Ryan MJ, Levine MM, Nason M, Nohynek HM, Plotkin S, Rees H, Singh JA, Swaminathan S. Placebo-Controlled Trials of Covid-19 Vaccines - Why We Still Need Them. *N Engl J Med*. 2021 Jan 14;384(2):e2. doi: 10.1056/NEJMp2033538. Epub 2020 Dec 2. PMID: 33264543.

> ments for participants who desire to obtain a different investigational vaccine. People who enroll in clinical trials for altruistic reasons would probably understand the value of gathering data . . . .

Again, the same argument as that from the NIH appears in the WHO: the idea that the research participant's own health should somehow default to exigencies of science. We return now with the WHO to the place where the NIH was in July 1997:

> Countries with limited or no access to a known effective vaccine could thus ethically permit placebo-controlled trials of vaccines of potential relevance to them even if effective vaccines were already being marketed elsewhere.

In a world where we have been repeatedly been told that there are Covid-19 vaccines that are highly safe and highly effective, where we have been promised solidarity and equity, our leading public health institutions are using ethics to argue for the hegemony of political and financial interests in research on human subjects.

4. Vaccine nationalism and vaccine diplomacy

One of the failures here is in the very title of the United Nations. We speak about "vaccine nationalism," but what we have failed to discuss during this webinar is "vaccine diplomacy."[18] We now see the international community, often with the support of international ethics bodies, using those terms differently for different countries. One is as derogatory as the other depending on the context in which one or the other is used, but both are present around the world, in high-income countries, in middle-income countries, and in low-income countries. The solution to this nationalism that has so inhibited our ability to move beyond our own specific interests, including in ethics, is not more nationalism. That is not the solution. Neither is the solution more "internationalism," a solution that inherently is nationalistic in its approach. Ethics should look to provide a corridor for critical reflection that amounts to more than scientific, political, and economic considerations in health-related research and public health measures during this Covid-19 pandemic. Why did it not do so?

What have we seen at the patient level? Let us consider people, individuals and communities. Let us consider their interests, their needs, and their ambitions. This is the place where ethics should be. We have seen a reluctance for patients to come to hospitals for scheduled clinical trial visits[19]. We have seen a reluctance for patients not just to come to hospitals for clinic trial visits but also for care: for cancer treatment and care, for cardiac treatment, for rare diseases, and a whole host of normal healthcare care[20]. We have seen a sig-

18) Gruszcanysk, L., & WU, C. (2021). Between the High Ideals and Reality: Managing COVID-19 Vaccine Nationalism. European Journal of Risk Regulation, 12(3), 711-719. doi:10.1017/err.2021.9. See also: Iftekhar EN, Priesemann V, Balling R, Bauer S, Beutels P, Calero Valdez A, Cuschieri S, Czypionka T, Dumpis U, Glaab E, Grill E, Hanson C, Hotulainen P, Klimek P, Kretzschmar M, Krüger T, Krutzinna J, Low N, Machado H, Martins C, McKee M, Mohr SB, Nassehi A, Perc M, Petelos E, Pickersgill M, Prainsack B, Rocklöv J, Schernhammer E, Staines A, Szczurek E, Tsiodras S, Van Gucht S, Willeit P. A look into the future of the COVID-19 pandemic in Europe: an expert consultation. *Lancet Reg Health Eur*. 2021 Sep; 8: 100185. doi: 10.1016/j.lanepe.2021.100185. Epub 2021 Jul 30. PMID: 34345876; PMCID: PMC8321710.

19) Sathian B, Asim M, Banerjee I, et al. Impact of COVID-19 on clinical trials and clinical research: A systematic review. *Nepal J Epidemiol*. 2020; 10(3): 878-887. Published 2020 Sep 30. doi: 10.3126/nje.v10i3.31622.

20) Rosenbaum L. The Untold Toll - The Pandemic's Effects on Patients without Covid-19. *N Engl J Med*. 2020 Jun 11; 382(24): 2368-2371. doi: 10.1056/NEJMms2009984. Epub 2020 Apr 17. PMID: 32302076.

nificant delay in patients presenting for diagnosis and treatment across the board, including Covid-19, but in many other diseases. And we saw a dramatic shift in the pharmaceutical industry and in the public health community towards its response to Covid-19 and away from non-Covid-19 clinical research [21]. Our entire healthcare systems became Covid-19 focused, completely dominating all other healthcare provision, including our mental health provisions.

5. Poor selection of trial cohorts

One of the things that we have seen with regard to Covid-19 is a poor selection of trial cohorts. *Lancet Global Health* reported in May 2021 that the global collective clinical trial response to Covid-19 has occurred with inadequate collaboration between researchers [22]. Inconclusive research findings from many clinical trials have re-emphasized the importance of high-quality clinical trial research [23]. Our science has slipped. It has not become better because of Covid-19. It's become more politicized [24], more nationalized, less cooperative - less cooperative in the field of science, less cooperative in the field of data, and less cooperative in the field of ethics.

The medical research response to Covid-19 has been inefficient and wasteful. The pharmaceutical industry is at fault, but not only this industry, these researchers. The report indicates that we have seen this across the medical world, across researchers and not only in first-world countries. We have seen an overwhelmingly large number of clinical trials having been registered and done with questionable methodological quality. The Covid-19 pandemic has highlighted the need for more coordination and collaboration, but how we are to achieve this coordination and collaboration, that we still do not know.

6. Lack of preparedness

Fundamentally, what this pandemic shows us is that there has been a lack of preparedness, a lack that we cannot limit to only this pandemic or potential future public health emergencies. Fundamentally, we have failed to recognize that this radical disruption in our societies was caused not only by a virus, but even more so by our responses to it. This calls for basic changes in how we carry out research and in how we perform

21) Iftekhar EN, Priesemann V, Balling R, Bauer S, Beutels P, Calero Valdez A, Cuschieri S, Czypionka T, Dumpis U, Glaab E, Grill E, Hanson C, Hotulainen P, Klimek P, Kretzschmar M, Krüger T, Krutzinna J, Low N, Machado H, Martins C, McKee M, Mohr SB, Nassehi A, Perc M, Petelos E, Pickersgill M, Prainsack B, Rocklöv J, Schernhammer E, Staines A, Szczurek E, Tsiodras S, Van Gucht S, Willeit P. A look into the future of the COVID-19 pandemic in Europe: an expert consultation. *Lancet Reg Health Eur*. 2021 Sep;8:100185. doi: 10.1016/j.lanepe.2021.100185. Epub 2021 Jul 30. PMID: 34345876; PMCID: PMC8321710.

22) Park JJH, Mogg R, Smith GE, Nakimuli-Mpungu E, Jehan F, Rayner CR, Condo J, Decloedt EH, Nachega JB, Reis G, Mills EJ. How COVID-19 has fundamentally changed clinical research in global health. *Lancet Glob Health*. 2021 May; 9(5): e711-e720. doi: 10.1016/S2214-109X(20)30542-8. PMID: 33865476; PMCID: PMC8049590.

23) Rodgers, F., Pepperrell, T., Keestra, S. et al. Missing clinical trial data: the evidence gap in primary data for potential COVID-19 drugs. *Trials*. 2021; 22(59). https://doi.org/10.1186/s13063-021-05024-y.

24) Crabu S, Giardullo P, Sciandra A, Neresini F (2021) Politics overwhelms science in the Covid-19 pandemic: Evidence from the whole coverage of the Italian quality newspapers. *PLoS ONE*. 16(5): e0252034. https://doi.org/10.1371/journal.pone.0252034.

public health interventions. We need to implement research and public health measures based on true evidence carried out in scientific frameworks that allow us to evaluate those interventions.

Here in Belgium, we see every night on television and nearly every hour on the radio how imperative vaccines are. We are told about which percentage of our population has been vaccinated. We are told about how scary it is to go out on the street without a mask. What we do not hear on our news is that our emergency rooms at night are full: they are not, however, filled with Covid-19 patients; they are filled with acute mental illness patients. We do not see on the news that in Belgium there is no room in a hospital for patients with mental illness, that critical operations are delayed, or that there is no room in care homes for patients with mental illness. We never had this situation before.

7. Ethics found marginalized in the Covid-19 response

Did ethics play a role in the Covid-19 response? Ethics appears to have played no role at all. Ethics was and has been for all practical purposes marginalized. “Ethicists” lent their support to insufficiently prepared research and public health measures not based on evidence. They lent their voices to decisions largely taken on political, economic, and investment bases.

Probably the role of investment has played the largest role in this public health response to the Covid-19 pandemic. It is not just about high-income countries and low-income countries. We have poor people in Belgium. We have people in Belgium who have no access to any kind of healthcare. We have poor people around the world. Through our response to Covid-19, we are increasing the amount of poor people in the world, and we are increasing wealth of the wealthiest. “Philanthropists” who have carried great influence in our international organizations, our national responses, and media reports in directing the Covid-19 response have at the same time increased their grotesque fortunes. Governments too have acted largely in the interests of the powerful, including those holding influential positions in agencies and academia. It is not just the pharmaceutical industry that should give ethics pause for reflection during this pandemic.

> Pandemics, like natural disasters and austerity, reveal that we are not all in it together. There is instead an uneven capacity to act and react for some while opportunities abound for profiteering by others [25].

Further, we need to appreciate that preparedness in ethics is not just for this pandemic and potential future public health emergencies, but it is fundamentally about recognizing that the radical disruption caused by a virus (or another unexpected health emergency) and our response to it brings with it a requirement for basic changes to how ethics and the community of ethicists comport themselves to society, governments, and powerful international public health and economic organizations.

8. Why ethics failed?

Ethics failed because of the structures of power in our communities, in our societies; ethics failed because

25) Klaus Dodds, Vanesa Castan Broto, Klaus Detterbeck, Martin Jones, Virginie Mamadouh, Maano Ramutsindela, Monica Varsanyi, David Wachsmuth & Chih Yuan Woon (2020) The COVID-19 pandemic: territorial, political and governance dimensions of the crisis, Territory, Politics, Governance, 8: 3, 289-298, DOI: 10.1080/21622671.2020.1771022.

it sought a place of power in politics, science, and public health rather than critiquing the cost of using a pandemic to pursue power and wealth. Ethics also failed because of the scientific and public health communities, a dramatic failure of science and public health during this pandemic. Ethics failed principally because of the ethicists themselves: because ethicists failed to have the courage to critique public health decision making and move beyond the comfort of a staid discourse on guidelines and equity. There has been no place for ethics in the public-health decision-making and there still is no place for ethics in public-health decision-making. It is not that ethics suddenly took a backseat.

> Without global solidarity, this virus cannot be defeated. It spreads when we don't cooperate and when we look inwards instead of outwards and trying to help each other.
>
> Tedros Adhanom Ghebreyesus, Director-General, World Health Organization (February 2021)[26)]

The WHO Director-General is correct: science and public health fail when they fail to follow their own evidence, their own maxims. Ethics too needs to heed this warning. Ethicists themselves have not stepped back and asked with true reflection: What is ethics about? Why is ethics important to the discussion? What role should ethics play? Ethics failed because it wanted so hard to measure up to the science, a science that lent its support to decisions largely taken on political, economic, and investment bases. Ethics failed to measure the science against its own principles and maxims. This failure bears with it monstrous impacts for individuals, communities, and our global society.

Acknowledgement: Learning in the margins

(November recognitions just prior to publication. Lest we forget the pathways that brought us to this interim in time.)

I wish to express my appreciation to those who most helped me examine and appreciate the role of ethics these past 18 months as the world comes to terms with a health and science crisis. As the COVID-19 pandemic unfolded in early 2020, a global group of ethicists, public health professionals, scientists, and socially engaged persons came together under the heading 'Preparedness Planning for Clinical Research During Public Health Emergencies (PREP)' to share their knowledge, experiences, and questions in order to learn, perform better in their institutions, and write and teach with greater understanding and sensitivity. It was the largest and most inclusive grassroots gathering during this period. Facilitated by the Good Clinical Practice Alliance – Europe (GCPA), the Strategic Initiative for Developing Capacity in Ethical Review (SIDCER), and the MRCT Center of Brigham and Women's Hospital and Harvard University, the group met weekly for a year on an open virtual platform that welcomed participants from every continent having more than 50 countries represented. We had the opportunity to receive reports from, and discuss with, experts from the WHO, WHO-AFRO, PAHO, CIOMS, UNESCO, the US OHRP, the EU EMA, the UK MHRA, FPM-RCP, Nuffield Council on Bioethics, INSERM, DNDi, Drug Regulatory Authority of Pakistan (DRAP), Ghana Food and Drugs Authority, AVEREF, Research Data Alliance (RDA), FERCAP, FERCI, GO FAIR, the Cochrane Group, Epidemic Ethics, COVID-19 Clinical Research Coalition, The Pan-African Clinical Trials Database, Union of the Help and Support for Patients (Russian Federation), Center for iPS Cell Research and Application Kyoto University, Japan, and others. In the context of the emerging and often confusing global health security crisis, we examined clinical trials on vaccines and therapeutics, pediatrics research

26) WHO chief calls for global cooperation, solidarity to tackle COVID-19 pandemic. Xinhua. 2 Feb 2021. http://www.xinhuanet.com/english/2021-02/20/c_139753261.htm

and care, databases and data sharing, observational research, research on recent epidemics, oral health research, research in the social sciences and anthropology, and current developments in ethics review, informed consent, vaccine passports, and the political, economic, social, and ethics structures that were so determinative for global, regional, national, and local heath in times of a crisis. The group delved into the effects of COVID-19 on diseases of poverty, rare diseases, cancer, and general access to healthcare. The ethics review systems on every continent were discussed, with specific attention given to assisting countries in reviewing, evaluating, and adjusting their ethics review structures and procedures. Several research projects were carried out by the group, including into the attitudes of healthcare workers, a global survey of ethics review practices and interests, and the drafting of global guidance to support ethics committees during this challenging time. The role of the Declaration of Helsinki, the CIOMS guidelines, regulatory decisions, and the International Health Regulations were weighed in the framework of decisions being taken by governments and international organizations as we considered national and local impacts. This was an exercise of ethics in the margins: respectful listening to voices from diverse backgrounds and perspectives, and the building of friendships across divides. The learnings provided in the remarks above are deeply indebted to those voices who animated that open and transformative discussion. Global Friends of PREP continues to meet monthly facilitated by the GE2P2 Global Foundation. All are welcome to attend. Contact: David R. Curry (david.r.curry@ge2p2global.org).

A special thank you is due here to the organizers and editorial teams, who did an extraordinary job in conceiving this discussion, bringing the experts together, and editing and translating the proceedings for these reflections on ‘COVID-19 and bioethics: Pandemic and research ethics－Democracy, placebo and post-trial access’.

(Published November 15, 2021)

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Discussion (Day 2 No. 2)

Chieko Kurihara

Specially-appointed Professor, Kanagawa Dental University, Japan

Thank you very much Prof. Dirceu Greco for your powerful presentation. We learnt so much from Brazilian experience to battle with the difficult situations. We learned there are many things that bioethics can do. Japanese don't have such kind of experience, but we have to make such efforts. Thank you, Dr. Francis Crawley, for your excellent comment and analysis on how ethics can do in this difficult situation.

Ruth Macklin

Distinguished University Professor Emerita at Albert Einstein College of Medicine in New York City, the United States

Prof. Greco made an excellent overview of these many international documents, bringing in more than I had even remembered. Also, I liked the point about the weakened wording in some of these documents from one iteration to another. Of course, none of the provisions of these various guidelines are binding on anyone, but many countries do state their adherence to the provisions.

My question is, basically: are there too many guidance documents? Which ones should anybody - any government or any individuals - adhere to? People can pick and choose which ones they prefer or agree with more than others.

I note for the audience (if they are not familiar with it) that many years ago, the U.S. FDA (Food and Drug Administration) stated its adherence to the Declaration of Helsinki, but once a revised version of Declaration of Helsinki came out with specific wording on placebos (1996 and 2000 versions), the FDA didn't like that because the FDA loves placebos, and so the FDA pulled out and no longer adhered to the Declaration of Helsinki [1]. With all this picking and choosing, how valuable are these international documents, which say many good things but that very few people pay attention to?

Dirceu Greco

Professor Emeritus, Infectious Diseases and Bioethics, Federal University of Minas Gerais, Brazil

We have been together many times discussing these documents and I quite agree with Prof. Macklin's positions. The plethora of documents is a reason for mentioning Bobbio's saying about the fundamentals of human rights. What can one do? Just choose one or the other? We may say, I do not like the contents of this one, so I am going to get another one.

I am going to take this opportunity to say two things. The last discussion of the UNAIDS/WHO Guidance

1) Food and Drug Administration. Human subject protection; foreign clinical studies not conducted under an investigational new drug application. *Fed Reg*. 2004; 69; June 10, 2004: 32467-75.
http://edocket.access.gpo.gov/2004/04-13063.htm

Document[2] was just before the beginning of this pandemic. It was in Switzerland. Prof. Macklin, Dr. Otmar Kloiber and I were there, and I was very uncomfortable when someone presented in that meeting one guideline from the U.S. National Institutes of Health. We were discussing international UN (United Nations), WHO (World Health Organization) documents and a particular guideline from National Institutes of Health was included. What I mean is that there are so many guidelines and one way out to protect ethics and human rights is to have one specific for the country, including all what is needed for their protection.

But that's very difficult, because in many places, and I am going to go back to the National Institutes of Health again, most of these projects are international. And several are financed by them. They may put whatever they want. It's very hard to go against. We have this opportunity here. We have now here 46 people. I hope that we come together, think about that, and see what we can do as a group in all the venues that we participate naming to have one international document which could be binding. That could be from the United Nations/WHO as they had so many others. Maybe they still are not that much respected, but they could be binding for people to follow them. That's the first thing.

I am going to show you one thing that Prof. Macklin mentioned. In 2006, the FDA decided to take the Declaration of Helsinki out[1], out of foreign studies not conducted under an investigational new drug application (IND) because apparently, they were afraid that a new version was going to be very strict to them – their proposal was opened up for people to make comments. Of course, I made comments, Dr. Lurie made comments[3]. Prof. Ruth Macklin, of course, made comments. They didn't care. They just decided that "*later this year, the US Food and Drug Administration will adopt new standards of human ethical clinical trials conducted without its advance sign-off in foreign countries*." This took out the Declaration of Helsinki and they recommended that just the Good Clinical Practice document be followed. The GCP is not an ethical document.

Dr. Lurie and I published a paper in the *Lancet*[3] where we said that "*the Declaration of Helsinki is the standard bearer for international research ethics. It would be tragic if the US tendency to arrogantly flout international mores claimed the declaration as another victim*". I reckon it was a good paper, but no repercussions. But just a little bit later, there was an editorial in *Nature*[4]. It was very interesting because it was very much against FDA position. But they did not care. They do whatever they want, because again they have the power, they have the money. We have to keep fighting.

Ulf Schmidt

Professor of Modern History, University of Hamburg, Germany

I still think this is the absolute amazing meeting here and the debate we had over the last 2 weeks I can only commend you for having brought all these experts and played this together.

Let me just comment on some of the things which was said in the last two papers. Prof. Macklin is obviously absolutely right about the number of different codes and guidelines which the world has today. In the mid-1990s, Professor Troiler from Basel once looked at the number of codes which existed at the time, and

2) Joint United Nations Programme on HIV/AIDS and World Health Organization; 2021. Ethical considerations in HIV prevention trials. Geneva; 2021. Licence: CC BY-NC-SA 3.0 IGO.
https://www.unaids.org/sites/default/files/media_asset/ethical-considerations-hiv-prevention-trials_en.pdf

3) Lurie P, Greco DB. US exceptionalism comes to research ethics. *Lancet*. 2005 Mar 26-Apr 1; 365(9465): 1117-9.

4) Trials on trial. *Nature*. 2008 May 22;453(7194): 427-8. doi: 10.1038/453427b.

he counted something like 300 medical ethics codes in different fields of expertise. You can probably gather from even that the problems for scientists and experts to navigate that mass of documents and know which one was relevant for them. One of the results of that was obviously that the Declaration of Helsinki has become an increasingly a point of orientation because of that confusion in the field. That's a very important point being raised.

The other point which came through very well and I commend Dr. Francis Crawley for bringing up the issue of ethics and the failure of ethics in the current public health crisis. What is interesting in the current situation is that we have a discrepancy here between bioethics on the one hand which is historically largely and has been shaped by a western perspective, the discipline itself as it evolves from a post-war period, and was established in universities and as a field of professional activity on the one hand and the lack of development of something what one could call public health ethics. That is an area which is underdeveloped conceptually and historically, and what Dr. Crawley was highlighting here is the lack of recognition that ethics need to play a part in public health to a greater extent as how ethicists have ever really conceptualized that and engaged with.

Finally, a very important point he made, in relation to international cooperation which was obviously a very, very great importance after the Second World War and the whole creation of international institution and organizations from the WHO to the WMA and others are testament to that cooperation, we are obviously seeing a major failure in cooperation and collaboration and one may obviously ask whether this is only due to populist politicians and that we could say, the world has just had bad luck. At the moment when the pandemic struck, we were given a bad hand so to speak, as far as the international politicians are concerned, but the reality is slightly more complex than that.

What I want to highlight is perceptions of different communities, how they see themselves. Dr. Crawley highlighted that there was a failure of science. Before joining today's discussion, I was in a workshop with top scientists, top virologist, and the perception is a complete different one. It is literally one of complete success. Scientists think that they have achieved the greatest success in this pandemic by collaborating and developing vaccine so quickly. What I want to highlight is that there seems to be very different ways of perceiving this pandemic in different communities, and this meeting has very much highlighted the issues which are of fundamental importance at various levels of our debate.

Otmar Kloiber

Secretary General, World Medical Association

First, let me thank you for bringing this together as the previous speakers did. It's a very interesting and very important discussion we have here. I would like to quote an American writer, Damien Barr, who has written a poem about the Corona pandemic. Let me give you some of his lines which are so important. He wrote, "I heard that we are in the same boat but it's not that. We are in the same storm, but not in the same boat". Later on, he said, "some are on super yachts and some have just one oar, and I may add, some are sitting on the sundeck and some are about to drown." What this pandemic revealed is just the ongoing inequity which we are seeing in this world It is nothing new. Aren't there some fundamental things that we have to change and that we have to address?

Some are just bashing the pharmaceutical industry, all the richness and profits they have made and praising some of the healthcare systems. But it's not that easy. Yes, there is a failure that is going on for many years

for instance, that our international cooperation is based on agreements that favour money-making but not the people.

We have agreements like TRIPS (Agreement on Trade-Related Aspects of Intellectual Property Rights) and GATT (General Agreement on Tariffs and Trade) which are arranged around economic systems with the idea, that if you allow more profit, more trade, more business, then everything else will follow and there will be more justice and there will be more wealth for everybody. We have learnt that it is not that easy and there is no guaranty that more economic cooperation improves the situation of the people. However, that doesn't mean that we shouldn't cooperate. It doesn't mean that we shouldn't trade, but the question is whether the ideas on which we have based all those cooperations are the right ones. Whether the primacy has to be on we are doing business and then everything will follow or whether we should ask, what people need and how do we do this in a fair, in a just way. But those questions have never been asked. If you look at the very recent past on treaties that have been negotiated again, those treaties are not favouring the poor of this world or even a fair dealing with those. It's still this mentality of us against the rest of the world which is prevailing.

Is there hope to think that politicians alone will do this? Let's be serious. What we have seen during the last 18 months has not been a hallmark of political achievements - in nearly no country of this world. Yes, some have been better prepared but those are now falling back quite obviously because they have missed the opportunity to engage in vaccination and in doing the next steps. In most other countries, politics has failed. The Secretary General of the United Nations Mr Guterres is completely right. It has failed. Is that only to blame politicians? No. We have nice papers at the World Medical Association that described exactly the situation that would come up with a pandemic. We have asked for pandemic preparedness, but what have we done? We have not insisted. We were not standing on the feet of our politicians saying you have to change that.

Prof. Ames Dhai quite rightfully spoke about moral bankruptcy. That is a very strong term and it is correct. But on the other hand, is there a different behaviour in those countries which are in need? Look at the situation in Africa? A lot of governments seem to be more interested in engaging in the next war with their neighbours than providing healthcare to their people.

The underlying problems are those of inequity. Those we have to address. We are not getting a quick fix for this pandemic. That will not be possible, but we will have to focus on what we do next and how to continue. There is a strong role for civil society and for scientists to remind our politicians that we need different treaties, that we need a different system for intellectual properties. Just waving our patents does not make a big difference. We need a new system of how we deal with intellectual property and what we think is the common good and what is not. Thus, there is a role for civil society to engage more, a role for all of us, whether you are a scientist or activist or you are providing humanitarian help. We all must push much harder on our politicians, to remind them that inequity has to be fought. That's not easy.

Let me just tell you coming from a rich country, from a country which on an international scale has done pretty well with the vaccinations. What the people demand and what they charge my health minister for in Germany is not that he is considering providing more vaccines to other countries. They are lamenting that he has not bought enough vaccines for Germany. That is what they are excusing him of as a failure, not the concerns about third countries. He indeed may tell you that he has sworn an oath to protect his country, not to protect other countries. In the thinking of global health and global inequity, we have to advance the

political system a big step forward. We must get better prepared, but the preparedness has to be on all levels, and it has to be with the engagement of all of us, not only of the industry, not only of the politicians. If we don't all engage, it will not change.

Tammam Aloudat

Managing Director, Global Health Center, Graduate Institute of International Development Studies, Geneva, Switzerland

There is obviously a pragmatic point that comes from a civil society organization like MSF which historically working on access to medicines comes from the fact that we have patients that we cannot afford to treat, even as a western relatively rich organization that comes from the HIV pandemic and the exploitative way the early days of anti-retrovirals were. But that obviously is one part of it and we have engaged over the years with many access issues and faced the consequences of the inequities that have been addressed, and there have been directions that debate the necessity for the exploitative intellectual property regime which allows by design and by definition a highly manipulative system to recreate and reinvest and reinvent medicines that are by definition created to be profitable before being anything else, the exploitation of public resource and so on, and then the demand of poorer countries to work against their own populations by making them enforce IP regimes that aren't of their interest. But it also extends to research and development. It extends to the fact that many of the medicines that get patented are developed publicly and so on.

But then if I take my ex-MSF hat aside for a second and I try to follow up on Dr. Crawley and Dr. Kloiber's comments, Dr. Crawley talks about the position of ethics. Again, like much of the academic disciplines, there are first way too many directions to be followed usefully in an applicable way for a practitioner and an advocate to do. I will just give an example of where the starting position of an ethical argument has been fairly disappointing. A few years back, there was an article in the *Lancet* by Persad and Emanuel [5] argued that in the interest of coverage and from an ethical point of view, we should promote the use of second-line, less efficacious more toxic medicines in sub-Saharan Africa.

In that position, the ethical stand was to give worst medicines because they are poor, and we have tried to answer that. The fact that this ignores what makes people poor and how is this becoming a double punishment. For their poverty, they get worse healthcare by design, not by necessity, and that is dressed as an ethical position. It takes me back to that it's the starting point that matters. Dr. Kloiber has talked about equity, and he made the point of the waste and conflicts in Sub-Saharan African and African countries that are wasting money. That is probably technically true, except that reflects a point that ignores the historical context that has put them there and the fact that they don't buy weapons from outer space. They buy them from liberal democracies that continue to do that - this dismembering one inequity issue from the political and from the geopolitical context and allowing this invention of innocence of liberal democracies. In the World Health Assembly 2 years ago, it was liberal democracy, Canada, Norway, Germany, UK, who opposed a resolution in transparency. The same countries opposed the waiver today. There is a consistent acceptance of the imbalance as the norm from which we start our moral positions. That is unchallengeable.

It is troubling that this is where we are now, because if we are going to talk about beyond waiving IP (intel-

5) Persad GC, Emanuel EJ. The ethics of expanding access to cheaper, less effective treatments. *Lancet*. 2016 Aug 27; 388(10047): 932-4. doi: 10.1016/S0140-6736(15)01025-9. Epub 2016 Apr 20. PMID: 27108231.

lectual property) issues at pharma, then at least as someone who has no leg to stand on among ethicists like yourself, I need something that takes me beyond just it's not only the job of politicians and pharmaceutical companies. It's all of our jobs. When something becomes everybody's responsibility, it becomes nobody's responsibility, and that is very difficult to deal with in any practical manner. Until we have that, forgive us if the obvious targets are pharmaceutical companies and politicians who are the direct harm, who are the ones who are linking aid to trade, who are the ones who are putting profit above all, and who are the ones who are doing it with very little shame and cover when things hit the fan.

Greco Yes, I want to second Dr. Aloudat, but I want to stress against something that have been said before. Much of the ethics is not involved in all of these. Maybe the ethics as an institute, but all of us are people that are working ethically trying to make a difference. I can say and I am repeating what I have already said what has happened in Brazil in the last 40 years, when it was decided to face frontally the AIDS epidemic - different from what Dr. Aloudat said, we decided to provide drugs for everyone. We have a problem that many of you have difficulty in accessing what we publish because we speak a language that most do not understand. If we publish in Portuguese, you don't read. Many things that happen in countries like mine are not as publicized as for instance what comes from South Africa, as they publish in English. Repeating again Brazil has been at a time a very good case study example of how to face things with the participation of civil society, as it happened in the confrontation of the AIDS pandemic.

I am going to quote Dr. Kloiber but in a different way. We are here in the same storm, but pharma is in another boat and maybe this is the worse part of the problem. As Dr. Aloudat said, it is very easy, and I do that all the time in Brazil, to blame the government for everything that is happening there. Of course, they are a substantial part of a problem, but we are part of the solution. The problem is that we are in a small boat. We have to join together to make the emancipation that we have been saying all the time to happen. I am going to use the example again when in 1988 Brazil decided to establish one only public health system for everyone. And the Brazilian Unified Health System (SUS) was created. Is it fantastic? Of course, it is not, but it's amazing to think that currently over 200 million people have access to one public health system for everyone. That's a good start. I must use all those examples from developing countries to say that it's possible and I agree with Dr. Aloudat. Our biggest target now this moment is pharma industry. It's not the only one. It's not going to be the solution even if we succeed. Even if we find a way of suspending or much altering the TRIPS agreement for health products, it will not make a big difference now, but it will be a good start. It will certainly be a significant step forward, something that we can do as people together, and this debate is an example. We have people from many places in the world, but even if we don't have tha power to do that at once we together will make a difference. And this movement can sow the necessary seeds.

For instance, when Prof. Kurihara and myself, one in Japan, another in Brazil, decide to do things like that together, it's a small plant that we have to keep growing, keep watering to see what can happen aiming at changing the status quo. I am not naïve on that. It's not going to be easy. It's going to take time, and maybe the COVID pandemic could be another stepping stone, because people all over the world are talking about unacceptable situations that were pre-COVID, all the inequity, the lack of access, the neglected disease, they were there before, and COVID just put it on stage, in the spotlight. We have to use that now to see that the end of this pandemic will not mean just returning to what we had before.

Francis P. Crawley
Good Clinical Practice Alliance – Europe (GCPA)
Strategic Initiative for Developing Capacity in Ethical Review (SIDCER), Leuven, Belgium

I thank the participants for the excellent conversation this webinar has realized. It has been timely and important. The webinar has shown that the first place to look when you look for failure is to look to yourself. We have had the courage to do here.

Rihito Kimura
Professor Emeritus of Bioethics, Waseda University, Japan

Thank you very much indeed for the wonderful symposium for 2 days since last week. We really appreciate all the speakers' very important comments. We are not having open conversations like this in Japan yet. I really enjoyed the event and we seriously considered what is the basic starting point of bioethics after the war. I had an impression that we have to go back to the fundamentals, we have to go back to the roots of the ideas, of the new medical ethics since the time of the Nuremberg Code, 1947 [6].

Last week, I talked about my thesis on the experience in Japan, and I think Dr. Schmidt has read this book. I have written on issues of the Japanese bioethical experience during wartime which has had a very negative impact to all the Japanese medical people, and I recommend one of the very important books in thinking of this bioethical development since after the war is this book, "Against Relativism" written by Prof. Macklin [7]. Bioethicist nowadays must read this very important book based on very good analysis of cultural elements. She mentioned the cultural diversity and the search for ethical universals in medicine. In this time of COVID 19, we need to see through the fundamental issues after the war and we have to review all the development of bioethics regarding time of this COVID-19 to find out new ways to proceed. I have received many interesting pieces of advice and suggestions during this conversation, and I really appreciate all people's participation with very good analysis, insight, and energy.

I really appreciated as a Japanese bioethicist to have this very important contribution from people from all over the world.

Greco It has been a pleasure to be with Prof. Kimura, Prof. Kurihara, Dr. Saio, Prof. Imamura, to meet all the Japanese group and other international colleagues. For me it has been great to participate in the continuation of our debate in 2019 in Tokyo. Even if the Brazilian Society of Bioethics was a part of it, it was a work spearheaded together, with a great input from Japan.

Let's hope that we can keep fighting against inequity, keep fighting for the people, even if we are not in the same small boat as most vulnerable people are. But we have a reason to keep the indignation together so that we can do even more than we have been doing. I thank you all and give the word back to you to say the last farewell. Thank you very much.

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6) The Nuremberg Code. Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, October 1946-April 1949. Vol. 2, p. 181-2.

7) Macklin R. *Against Relativism: Cultural diversity and the search for ethical universals in medicine*. Oxford University Press; 1999.