



Presidential Commission  
*for the Study of Bioethical Issues*

TRANSCRIPT  
European Perspectives

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**DR. WAGNER:**

We've got forty-five minutes to talk about the European perspective – we're going to take our whole forty-five minutes because we expect to be just as rich as the prior conversation was.

And I thought we had to – there she is. Our two speakers in this session, we'll begin first with Linda Nielsen. She is Vice President of the European Group on Ethics in Science and New Technologies and Vice President of UNESCO' International Governmental Bioethics Committee, also, Professor of Global Law and Governance at the University of Copenhagen in Denmark, and President of the Danish Cancer Society. She serves as Chairman of the Danish IT Security Council, and is a Member of the Board of Trustees of the Queen Margaret and Prince Hedrick's Foundation. She has been a member of the, of many commissions, including a Danish Globalization Council, Danish Finance Minister's Think Tank on Future Growth. She has been with us throughout our proceedings, and we welcome you to this panel. Linda.

**LINDA NIELSEN:**

Thank you very much.

**DR. WAGNER:**

There you go.

**LINDA NIELSEN:**

Thank you. Thank you for the invitation. It's been extremely interesting. And I hope to fit in with what has been already said and try to start a discussion on that. And it's so nice to be here, kindred spirits, and many other aspects from where you're sitting now and trying to get some inspiration, so I really hope to fulfill that.

What I have chosen to do is to say two things about the European approach, two things about the bill and the conference, and two slides about what do I think I can make use of; how can I inspire you in different ways. I hope to do that.

The first thing is that in Europe, we have the European Chart of Fundamental Rights. It's been adopted by most of the twenty-seven EU countries and it creates somehow the basis of what we're doing, like the UNESCO, like other things.

The first one is dignity. Respect for physical and mental integrity. Free and informed consent. And then a very European speciality, prohibition of making the human body a source of financial gain. The next one is freedoms, liberty, security and

private life, and protection of personal data. Then we have the equality, the non-discrimination principle, respect for cultural and religious diversity, and the one which is crucial for this one, the rights of vulnerable groups children and the elderly, and you could include other poverties right in that respect. Then solidarity, which is also important for the topics we are dealing with today. Access to preventive healthcare, the right to benefit from medical treatment is extremely important for us. High level of human health protection. And then we have some further about citizens' rights and justice.

Many of these, can be seen also in the UNESCO declaration and other kinds of declaration, and I suppose that we share them, the U.S., the EU and many other places. Of course, the problem is the balancing. If you're going to prioritize between the freedoms and the dignity, how do you do that then? And that will be part of what we are dealing with here today.

The next one is about standards, which kind of standards do we have in Europe? And this is an overview, so Maurizio will be much more elaborated about what's going on, so just to fill in the framework before discussing. But first, the declaration, and the UNESCO declaration, I'll say nothing about that, you have heard already.

Next is the Council of Europe by Ethics Convention. It covers more than the EU, it covers 41 signed European countries, or maybe a little more today. And it says about, something about consent, risk assessment, integrity, and privacy, including vulnerable groups. And what they say about vulnerable groups here might be of inspiration to you.

Then there's the EU directive on clinical trials. It's a minimum directive, which means that you should have fulfill it, but you could do more, each country, if you want to. It has provisions about consent, risk assessment, integrity and privacy, and also here about vulnerable groups. We have the EU Directive of Good Clinical Practice, you've heard about that, I'll say nothing about that. The EU Data Protection Directive, about privacy consent. And then a very specialty, also a European specialty, the EMA, the European Medicines Agency. And this is interesting because it has the ability to give opinions before the European Commission can grant marketing authorization. And in doing so they make sure that the ethics are taken into account. And this connection between ethics and marketing I think presents a solution which is very good in many ways.

Next one will be they are the blue ones. They are the Ethics

Commission, of which you are part, and just to make sure I've said what it's about, the EGE is an independent jurist and multidisciplinary body which advises the European Commission. Do you know that? That role? Very interesting role, don't you think so? That's not so.

And the next one is what we've said about clinical research in developing countries. It's a long opinion and I've tried to somehow put it into one slide with a number of pieces. So I had a chance to remember, I was afraid that I was supposed to talk without having my papers, so it's the only way I'm trying to remember to the, the name.

Protection of participants. The risk should be taken into account, of course. The consent, free, informed consent to be withdrawn at the end stage. Ethics Committee approval, both in the host country and the sponsor country. Treatment for the ones who go into the research, both if they are not able to get the treatment in the home country and after the research has ended. And then insurance should be secured. Pluralism, in the way that the local tradition should be taken into account, and the standards of both host and sponsor countries, just like we heard in the UNESCO declaration, we say this is a very important thing to do. So that we make sure that you cannot move to other countries because it includes list protection which will have to take both countries into account. If you don't have an ethics committee in the relevant country we try to say that then you can have a mixed committee of people of the host country and the sponsor country.

Partnership, take the host country into account, make real partnerships with them, and include local scientists from the very beginning to the very end. Secure capacity to building so that you make sure that this is being taken care of. Make sure it has an impact for society, and make sure that there are a share of benefits when you make publications, include the local scientists when you make patents, include the locals. et cetera.

The last one is real crucial. Protocols in publishing. That should be registration and information on what has happened, including negative results, which is very important. And then we have a long discussion about Placebo, I can go into that if you want in the questions, but I will not do it right here. And we opened it up, as I understand, and about relevance, it was said that it should be relevant for the country.

Today – this is from 2003. Today I must say I don't think this is realistic, in the very narrow sense we said, but we can come back to that in the questions.

Then, Linda's considerations from hearing you. This has been a real working document. I amended it last night after hearing the discussions, so that I could make sure to fit in to what you were talking about. I was wondering, we talked a lot about not only having the restraints, but also explain what's the good thing about it. And to make that open up front would also, benefit the ones who are doing it, but will also benefit the ones on the other side of the table, because they can ask, well, what's in it for me? And not for me just only as a person, but for me as a local, something, as a society, a country, whatever.

And I think that somehow if I try to think about the whole area of business ethics, CSR, Co-governance Corporate Social Conspiracy, in that respect, you said for a long time, "don't say yes to child labor." And we all said, "don't say yes to child labor." But then they found it was much fruitful to say yes to child labor, but make sure that there were schools and there were things for the kids to do, not to many hours, et cetera, et cetera. So the way of doing things, instead of just having one thing, then widening it up, what can we do for the local society? So both better, cheaper, and local benefits of other kinds could be included, but say it in plain language what's in it for you.

Counter right, what don't we want? What do we want to ban? We want to ban unproportionate risks and unscientific conduct. Which conditions should we make sure are taken into account? Consent with clarity and committee approval.

Cautious recreation, I would recommend protection and protocols and insurance should be part of that. Compliance should be taken into account including inspectors. We've seen that in the EU combinations. We have inspectors being sent out, does that, send out inspections- how's this going? So that we make sure that compliance is taken care of. And then last but not least a culture of collaboration, capacity building. Both in signs for the local community in developing countries, but also for ethics for all of us. We heard that yesterday. I mean if we're in the university, or a business, or a special business in doing these things especially, there should be an ethic and be educated in this. So ethics is not only for the developing countries, it's for all implied in this.

And my last one will be the process of business of content somehow. And we've gone through the processes. I've totally agree with Francis' transparency is very, very important. Not the only one, but one of the important things.

Top/Down and bottom/up, sometimes we think we should either have a top/down approach, making regulations with your heart, et cetera, or bottom/up. I think we need both. We need regulation from the top, very, very little regulation, but then tough and making sure that it's being complied with. So top/down and bottom/up, yes, two things that are there.

I heard yesterday a lot about bureaucracy. And I hear that in my home country, in the EU, and there is a bureaucracy, so going through all the detailed regulations and guidelines, et cetera, could we make them easy and understand them? And could we make less of them? That would be a good thing to do.

Prior I explained in the corporate social responsibility in business ethics, we've seen that, instead of saying, "do this," then we say, "you should do this, unless you can explain to us why you don't think that's good for this specific opportunity." Plus, as we've heard the context, the complexity makes a difference to make very hard things to comply. Explain what might be a process that we could introduce into this area.

Dialogue and principles, that's what we're hearing today. Framework regulation, in securing – there is a specific content in very few paragraphs and then some processes to be taken care of. And then harmonization, not unity, we should try to harmonize so that we all agree about the basic principles and then we can have the variety for doing things in different ways, in different countries and settings.

I was wondering that my last, could I do it like we have research animals? They have replaced, reduced, refined. Maybe we could put persons to have respect, responsibility and responsiveness. Thank you.

**DR. WAGNER:**

Thank you very much. Thank you. Our next speaker is Maurizio Salvi, Policy Advisor to the President of the EC, the European Commission. He is the head of the European Group on Ethics and Science and New Technologies Secretariat. Doctor Salvi also leads the Ethics Sector in the Bureau of European Policy Advisors. He chairs the EC Interservice Group on Ethics, and EU Politics. Secretary General of the EC National Dialogue on Bioethics, a platform that brings together National Ethics Councils from forty-two countries. He's published extensively in bioethics, ethics, and biotechnology and in the philosophy of biology. Welcome and we look forward to hearing from you.

**DR. SALVI:**

Thank you very much, Professor Gutmann, Professor Wagner. On behalf of the present European Commission let me express the gratitude for having been invited here today.

**DR. WAGNER:**

Good to have you, Doctor Salvi.

**DR. SALVI:**

And I hope that we can strength our links fruitful between the two sides of the Atlantic. I now click to the ten minutes, just respected. And I'm going to day to report to you about four main elements in my presentation.

First why ethics count in European Union policies according to the Constitutional Treaty, the Lisbon Treaty. The second, that Europe is sharing a system where hard and soft law apply in clinical trials insofar ethics review of them and ethics approval are concerned.

And the matter being proposed is to have a [inaudible] organizational bioethics process then hard law as a matter for this. But with regard to the content is soft law approach applying, and then the principle of subsidiary then the different case by case assessment of the clinical trials being analyzed.

And third the fact that all this system works also because it has been established a mechanism to monitor its implementation. In the three different phases the approval of the clinical trials, the implementation of the clinical trials to ethics, and also the output of the clinical trials in terms of product, medical product for example. IPR authorization of the marketing of medical products, with regard to ethics. I will be really quick in order to address all these items, but I'm open to question from all of you.

First, why ethics counts? We have in Europe now a new Constitutional Treaty. This Treaty is called the Lisbon Treaty. And one integral component is the Charter of Fundamental Rights that Professor Nielsen just reported. These are legally binding elements. And the charter is proposing a set of shared values. These shared values are just the kind of minimum denominator in this baring mechanism for all European Union policies, including the one that we research, clinical trials, marketing, patenting, and so on and so forth. This mechanism is advocated in the notion of Europe as a community value by all the different logistics, executive, and administrative powers. And here just reported

some quoting by the President of the European Parliament, the President of the European Council, World Member State Committee, and also the President of the Commission, their executive power.

The way how this is approached, and impacted is on a kind of holistic way. And we are talking here about our law. The fear on clinical trials, patent research, data protection, medical product, use of animal research, those are current policy design of new areas such as ICT, Security, Defense, and so on and so forth, are all now taking into consideration the role of fundamental rights protection in [inaudible] viewpoint.

As far as ethics in clinical trials, one element that is important to understand is that when we are talking about Europe, we are talking about a notorious, incomplete complex machinery. Clinical trials can be addressed and regulated in the European Union level insofar this is at the super national level, because there are interest and added value of approaching these uses of research internationally. Internationally meaning between members states.

On the basis of that the Treaty of the European Union is that they view things in specific power, and clinical trial is one of the possibility to be at the rest of the European level. But at the same time it is also recognized the principle of subsidiarity where public health and also local regulation apply when clinical trials are carried out.

All these mechanisms have to be integrated with this set of shared values and then the result is a quite complex mechanism in which there is already being mentioned by previous speakers, or logistic tools on clinical trials and good clinical practice and also on the good manufacturing of products. And also the establishment of sources that have a relevance for the ethics committee, such as common databases of clinical trials being approved, and also the mechanism of reporting on negative results of clinical trials. These elements are assessable of all the European Union level.

Talking about the specific legislation on clinical trials, and the role of ethics. The method that I just advocated in the beginning requires that there is an approval by an ethics committee. What this directive has done in 2001 was to institutionalize the role of the research ethics committee. And this was a new mechanism by EU law, and has created some consequences. But the method was requested in the fine, in terms of conflict of interest rules,

composition of the inter-disciplinary research ethics committee, but not about the content, or let's say the guidelines, that this ethics committee had to do.

The approach is that when the method is established then it would be on a case by case basis of this committee to evaluate the research trials, without having a prefixed set of norms that are universal or used in the standard way. The content of this mechanism is to refer to the existing normative approach at the UN or International level, the Council of Europe and so on and so forth. But what has also been requested by this directive is that when there is an international clinical trial it's not possible to have the approval of the trial when outside the EU if the same minimal standards requested in the EU are not applied.

At the same time there are specific norms, but here I'm not going into details because probably these are things that you may ask, otherwise we lose these four minutes I still have about this internalization of the mechanism. But one element that I want to underline to you is that this is not a finished process. The directive is under revision. There is an open consultation ongoing. And the new, or logistic proposal, to the Coalition and the Parliament Council is expected to be in 2012.

One element that was mentioned by Professor Nielsen, is one of the mechanisms to be sure that the ethics provisions are taken onboard. And this is done by the authority authorizing the marketing of European medical products. You can see that this authority has the possibility to attribute, or refuse their [inaudible] by member states licensing of medical product within the EU. They have to monitor that the good clinical practice provisions have been taken onboard and all the ethics review approvals have been taken. And this is a way to have a mechanism of all the things and the mechanism also monitoring. And this is not only for products resulting from clinical trials being done in the EU, but also internationally.

At the same time when the clinical trial is sponsored by the European Union, there is a legal basis on which the fundamental respect of basic principle is required. And an ethics review is a companion to the one carried out in all member states where the research trials is taking place by independent experts.

Then if we want to summarize why these ethics review of international and clinical trials is important, first is because it's requested by a kind of a holistic approach where ethics count much more than in the past. Second, because it's a precondition

of the EU research funding. Third, the EU research authorization and clinical trial authorization. Fourth, because the clinical, or the products resulting from clinical trials will be not authorized to be marketed, if this is not done. It will be not authorized to be patented, and at the same time there will be a mechanism also to implement auditing to see whether this conditions have been carried out, not only at the moment of the proposal of the trials, but also when the trials were done.

But with regard really the mechanism the commission is using, because of the social and cultural diversity which characterize Europe you should understand that we have different social cultural entities, we have different languages, and we have a common approach only on minimum standards, which are recognized and identified in the charter of fundamental rights.

Then what the commission is proposing to also the legislative frame is to facilitate local capacity, in the different European Union member states to the research that is commodity, and also where there are multi center trials with the other regions of the world. Then is an approach of capacity building of research ethics committees which characterize also this mechanism. At the same time the fact of respecting certain cultural differences. This is just to show you the legal frame, and the ethics frame. You recognize all the mechanisms, and all the conventions that have been mentioned today. But just let me say where there are sometimes some divergency, or where there are sometimes some difficulties.

First non-commercialization of human body is required by the EU legislation and the tissue banking directive. And this is also part of one article of the charter of fundamental rights. The interpretation of this principle can be different when there are multi-center trials, actors, and countries.

The nonprofit involvement of volunteers. The notion of compensations, exploitations, reimbursement, in particular with the less developing country, in terms of economic considerations, is really controversial and what is required by the U.S., the nonprofit, views. Informed consent procedures can vary. Data protection provisions are different because we have a strong legislation data protection, for example, it's not existing in some other region of the world. And then also the protection of vulnerable groups and the role of the research ethics committee at the local level.

This is just to conclude, just to say what I've tried to explain to you and happy to discuss is that Europe we have just met, where hard law apply to the mechanism. But where soft law apply to the content of the work of the research ethics committee. The case by

case approach is the basis on which all the authorizations and all the valuations of clinical trials on all international levels, are carried out. And this is because the mechanisms of subsidiary is one of the basis on which we work within the EU and with other regions of the world. And with that I'm just happy to respond to all the Commission's questions.

**DR. WAGNER:**

Thank you very much. We'll start with Doctor Michael. John, I got you.

**DR. MICHAEL:**

Okay, so these are both really wonderful presentations. And Professor Nielsen, you really provided I think a strong ethical framework and a blueprint for how research should be done, especially as more resourced regions of the world reach out to less resourced regions of the world.

But I'm looking at Doctor Salvi's presentation, I guess, you eluded to in a couple of slides, and maybe you can provide us a little more granularity, a little more detail on how the ethical framework the Professor described to us might be utilized in funding decisions on individual protocols. If you had equivalent scientific merit between two approaches and yet one adhered to more of the approaches that Professor Nielsen described, would those kinds of proposals be the ones more likely to be funded?

**DR. SALVI:**

I didn't report also on the role of the European Group on Ethics has played in the complex European machinery because otherwise the minutes weren't there. The European Group on Ethics is the only body, according to EU legislation, which can advise the European Commission in the fields of Ethics of Science and New Technologies. The opinions being issued then reference value with the regard of all the different policy designs, and also the evaluation of research trials, these finals by the European Unions.

In this sense the ethics frame which Professor Nielsen described, which is also reflected in the European [inaudible] on the clinical trials in developing country is used as a reference point for this case by case approach that I just described that when the research protocols financed by EU are analyzed by external experts. Then the European Group on Ethics has provided the reference, let's say the basis, and this is one of the element which is taken into considerations after the scientific evaluation of the research protocols, where there is a necessity including of adding international partners is assessed scientifically. When there is the ethics review of these protocols, this ethics reference is taken

onboard and assessed with the regard to the specific elements of the protocols being scrutinized.

In this sense I underline case by case studies. And this is done by external experts with a rotation mechanism. And we try to have not a kind of preconceived top/down approach in term of a set of norms that have just to be evaluated in terms of compliance by expert groups, but to have also a critical analysis of each protocols to be analyzed with the regard to ethics implication, the scientific things, and also the specific peculiarity in the country where the research is carried out. Then in this sense this is used.

**DR. WAGNER:**

Actually, may I take some priority here to ask a question? And perhaps it's one we could defer for the larger roundtable conversation. But Linda, you seem to address something that John here has mentioned before. He used the word cacophony, and you used the word harmonization, which would be just the opposite. But then you said, but not unity. And Maurizio, you also made reference to how you valued the set of minimum standards, but you didn't use the words, highest principles. And again we can share this more broadly, but I'm wondering, what is it that sort of goes without saying that I haven't heard yet that searching for some unity around highest principles would not be a valuable thing to do? Is it simply politically impossible? Or is there really a practical and a good reason for it?

**LINDA NIELSEN:**

I think there are two reasons for it. One is practical and one is another kind. The practical is that it's very difficult. For instance, when you had a problem with the Helsinki Declaration, because if I understand it correctly, the placebo discussion, or whatever, then I would say this discussion is so crucial that it's worthwhile that you cannot have harmonization between the bigger areas of the world because of that. I would say, "no." I would rather leave that to a lower level so to say.

And the other thing is that when I say that "why can't we have it all?" Then it's also because as many have stressed here today, and yesterday, you shall have to see things in context. Things are different in different kinds of countries. They are different for each research project and such. And to try to make them fit into one scheme I don't think that will be very helpful. And that's why I'm trying to introduce different kinds of layers where I only have some things in the top layer.

**DR. SALVI:**

Just also another consideration. The effect of having universal principle is already, we want to be realistic, on the table. The charter of fundamental rights of the EU is advocating principles that you can recognize in the UNESCO declaration of fundamental rights, for example, in the Council of Europe Convention. The effect is not the principle, it's how you implement the principles. And on this mechanism you have huge diversities. And the European Union recognizes diversity because it's composed by diversity. I underlined its social, cultural, religious, and linguistic diversity, the way we are. But at the same time if you go for minimal universal standards, you just have to consider that these have to be minimal. They should resolve from what is already on the table, and I mean the UN, the Declaration, the UNESCO, WHO, or the World Medical Association, they all have this common element.

Having in mind that the implementation phase of this, which translates into guidelines, is the level where the real differences appear and where the real priorities, also the different interlocutors, political, economic, private, et cetera, emerge. Then in this sense I wanted to respond.

**LINDA NIELSEN:**

It's also my impression from UNESCO, and we can have that confirmed, that the developing countries are quite happy with having these very broad principles, even if it's the lowest common denominator sometimes, and even if some say it's just [inaudible]. The principles are there, the consent is there, you can discuss to which kind, et cetera, et cetera, but it's there.

**DR. WAGNER:**

I would agree. And I understand the difficulties of a definitive document relative to the highest principles, or as you referred to them, as minimal standards. John, I think you're next.

**DR. WILLIAMS:**

Yes, thank you very much for two splendid presentations.

It's often said in the United States that the level of regulation, the level of complexity that researchers face here has led to, you know, massive off-shoring and outsourcing of research to developing countries in Eastern Europe, Africa, Asia. One distinguished researcher from Duke University came before us and questioned whether the United States was a fit place to do research these days. So the more demanding, the more complex your regulation of research, the less hospitable to research, you

know, how pharmaceutical companies view a particular region.

So you've described, I think, you know, two very excellent approaches to the regulation of biomedical research in Europe. And I'm wondering if you are facing the same sort of hemorrhaging, the same sort of rush to developing countries that we are. And if so are you doing anything about it?

**DR. WAGNER:**

I'd include Eastern Europe.

**LINDA NIELSEN:**

It's a difficult question. And I used to be a Vice Chancellor, so I know exactly what you're saying. We have a lot of persons coming to us saying, "this is much too complicated." And the interesting thing is that from Europe, many Europeans would say, well, we tend to go to the U.S. It's much easier there to make research. Much easier to make patents. (Laughter). Oh, yes. Absolutely. So that's where you start. And then you can say from there, there you can go to the relevant countries, to other places. So this kind of moving around during ...

**DR. WAGNER:**

In Europe.

**LINDA NIELSEN:**

Yeah, yeah. Well, I'm not saying that, that what you're doing is wrong. I would never dream of saying that, c'mon! But I'm just saying that this is what we sometimes, and the patenting is different, that's for sure. And valuing which is better? They're different.

But I think that somehow we shall have to take into account that this will always happen. And that's why at the end of the day the optimal thing to do is to get everybody onboard. We all know that will take a long time, if ever, but that's what we're trying to aim at. But we can't say that we won't have those principle costs, and we'll move elsewhere. I don't think that's a valuable document in a way.

**DR. SALVI:**

From Linda you will get the intelligent response. From me just, you know, the factual response about how this situation is.

With regard what is done by the European Commission, of course. What you have described is the fact that what is happening with European research being financed by the European Union. There is a growing rate of international clinical

trials going to these regions of the world. At the same time there is a need that has been recognized by the different research agency being associated to the program also to try to have sharing of information and common partnerships.

With regard to the ethical review of clinical trials, the reason why it has been requested in the European Union framework program that all research activities financed by the EU cannot countervene from the mental ethical standards, and principles, it was because having in mind this internationalization of research, it was needed not to have different standards in ethics for the European participants, and from participants from other regions of the world.

Then it was requested legally before having the financing that if there was an international partnership being established then fundamental ethics value, as described in the legal frame of the framework program, and the mechanism of monitoring, auditing all this, were to be established in the clinical trials insofar this was sponsored by the European Union public spending, different [inaudible] program.

What is now happening is that this current framework program for research is going to hand, because 2013 is then. We are talking about a budget of about 53 billion Euros. And now there is the current debate about the next framework program for research, and with an idea of adding substantial increase of budget.

The global dimension recognizes a priority, for both basic research and clinical research. And the need of having also a global debate about the relevance of ethics into this new dimension is recognized. And I just, you gave me the opportunity, to ask Professor Gutmann and Wagner to participate in September, we are going to have a conference with these forty-two countries about how the notion of our responsibility impacts into research innovation, including the clinical element of that.

Because we are trying to keep the link between ethics, innovation, clinical trials, and all different areas of research in a way that is all the time respecting of these global approach but also the respect of fundamental values. Then this is happening, is going to happen even more, and this is the response that at the moment has been done.

Bureaucracy is something everybody is just complaining for. And if you have seen in this light about the revision of the clinical trials

directive, one of the main criticism is the number of papers that have to be filled to have authorizations by this. This is something that we are trying to simplify, but is also a common complaint for everything which is done at the public level, at least in the UE.

**DR. WAGNER:**

Christine, last question before we go to the roundtable.

**DR. GRADY:**

I want to ask you something that you actually didn't address, but I hope that you can say something about. My understanding is that there is a fair amount of research, U.S. funded research that's collaborative with European collaborators, sometimes dually-funded, and maybe conducted even somewhere else in the third place. So my question to you is for research that is at least partially supported by the U.S. government, what are the biggest challenges from the European perspective? In terms of these kinds of issues? Human subjects' protection.

**DR. SALVI:**

In the slide introduced I said that there are some elements where some, I don't want to say differences, but where some diversity materialized.

These apply not only to these collaborative research in the U.S. but also in other regions of the world. Just to be precise, I refer that these free, non-profit participation on human subjects in clinical trials is required by the EU. There are other regulations which does not indicate that this is a precondition for an ethics review approval.

I indicated the fact that there are data protection issues. There are other regulatory frames in which the consent for the use of data, and for example, an epidemiological study and all these things for other uses than the consented one are not required. In the EU this is the case.

I refer the fact of protection of vulnerable groups. We do have reference in the program to the Council of Europe biomedical research protocol where the specific provision of protection of vulnerable groups are indicated. These provisions are not, let's see, identical everywhere in the world, in terms, in particular, of research involved incapacitated people, and several others.

I referred about open access. Open access is requested for all research protocols being financed by the European Commission. And this may be problematic for the patenting issue when private

enterprise are removed. Again this is not an element that is reflected in other regulatory frames.

I also referred about the need of having the approval of local research ethics committee as a precondition for patenting. Again this is not a requirement in other regulatory frames. All these elements are not a sign of a more sophisticated versus a more liberal approach, are just a sign of different regulatory frame coexisting. And these apply to the case you also have mentioned such as other international clinical trials where the co financing is foreseen with the EU and other regions of the world, from China, to India, to South America, and so on and so forth.

**DR. GRADY:**

One follow-up to that question. So is the resolution of that problem a case by case analysis as you said earlier? In other words, the fact that different jurisdictions have different rules about these particular items for example? How do you resolve that? Is it a case by case decision about whether it's okay to go?

**DR. SALVI:**

What this request is that the minimal ethics standard apply when there are also different actors, and I mean research centers in different regions of the world. The case by case approach is that having in mind that our law requires this to be implemented, it will be up to the ethics committee to evaluate according to the natures of the different clinical trials being evaluated, where in the countries where the research is carried out, this is the case or not. And then when there are the outputs, and I mean authorization of the market for medical products, or the licensing, or the attribution of the patent, it would be to their own committee about this independent about this to evaluate that the file is fulfilling this requirement.

And the case by case is the assessment of the different elements. Having a common line being defined even before the clinical trial starts, and even before, even different country research centers decide to make an application. If you want to do it, you have to follow this game, and then it will be evaluated.

**MR. WAGNER:**

Linda, did you have something very quickly to add?

**LINDA NIELSEN:**

Yes, very quickly. I think there are two elements in it. One is do we try to harmonize on the basic principles? Another is if you make a cooperation, we will then have the standards where you follow

both? Because if you have that, you still have your problem. And my question would be what do the U.S. researchers think about the European's?

**DR. WAGNER:**

No, that's fair. Well, again, with wonderful thanks to you. We'll now invite our first panel to join you, to join us together. And I'll turn this back over to our chair.