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All right okay so hi everybody I'm Peter Schwartz I'm the director of the

bioethics and subject advocacy program of the Indiana CTSI and we hold these

TREATs talks which are translational research ethics applied topics of course

is their aim to provide short ish introduction to ethical issues in

conducting translational research usually that arise out of a previous counsel we've had or question we've had

not always this one does arise out of a previous question that we've had repeatedly different

context and our presenter today is Jane Hartsock who is a visiting assistant

professor here at IUPUI in the medicine humanities and Health Studies program she has a JD a very extensive background

and health law and now in medical matters she is also our newest faculty

member in the bioethics subject advocacy program and so she like the rest of us are available for consultations on these

and other issues in the future and these treats talks are meant to provide an introduction and also an opportunity for

people who are doing research who may have questions to not only learn but also to call us if they have questions

with that further ado I'll turn it over to Professor Hartsock thank you hello I

am Jane we're talking that was a lovely introduction I don't feel like I need to add really anything to it so we thought

we could kind of move on so today we are going to be talking about that I think I

initially titled these problems of reconsent and I thought you know let's just be more friendly about it I'm going to

call it issues of reconsent in pediatric bio banking these things don't necessarily have to be problems it can

just be a sort of way of looking at the issue so that's what we're going to

talk about today and the particular issue that is under examination is under

what circumstances is a researcher required to obtain the reconsent of a

research participant who was enrolled in research as a child and has since obtained the age of majority so Mary

so that's what we're going to be talking about today and I like to kind of outline an issue at the front so we have

some boundaries on the conversation because there are lots of issues of reconsent that may pertain to adults but

we're going to talk about this within the context primarily of pediatric biobanking and children so we're going

to we're going to do that through three sort of objectives we're going to talk

about and we ran instead of kind of overview of bio banking within the pediatric context what is it and how is

it sort of different we're going to talk about the limits of the existing

regulations as to reconsent what I mean by limits is really the way in which

there is an absence of commentary in the regulations on this issue that leaves us sort of without a whole lot of guidance

as to what to do and then we're going to propose a framework for reconsent for

the examination of reconsent versus when waivers would be appropriate I had

originally kind of a fourth objective of examining future issues that might come up particularly with respect to the new

common rule but I think it makes more sense to just sort of drop the comments

in as we're going along and you can you know create the contrast as we sort

of examine this issue so biobanks for anybody who doesn't know there's a nice

clean definition of that by heroine Rothstein the bio banks are repositories that assemble store and manage

collections of human specimens and related data use to elucidate subtle connections between genetics and health

identify ways in which genetic variants contribute to illness and obtain powerful research results through large

sample sizes so bio banks in the United States can be

disease specific or not disease specific they take a lot of different forms NIH

is working right now to create a biobank for health-related data pertaining to

veterans which seems like a very interesting and useful project there are

also cancer related by open and many of those involve pediatric

research so file banks can store any kind of data really any kind of specimen

from plasma and genomic data they can be private or academic so they can take a

lot of different forms but most are academic and most get their samples from

forming relationships with hospitals either private hospitals or academic hospitals and then those samples come by

way of patients at those hospitals so there are more than 630 bio banks in the

United States and that number is growing particularly in light of the precision medicine initiative directed by NIH NIH

so thanks Obama almost all bio banks require IRB

approval before researchers can access specimen and when you talk about IRB

approval as most people have probably caught on by now this ends up boiling down usually into issues of consent how

do we obtain consent and properly advise people of what they are agreeing to do and what may happen with their

information if they participate in research so so bio baking scenarios can

take on sort of four primary forms I've got pediatric and parenthesis here because this is really true irrespective

of whether you have an adult or child but they can be actively collecting

disease specimens specific to for specific information so active meaning the person is the participant is being

used specifically for research and then bio banks actively collecting samples

and information from all persons without regard to disease data so not necessarily looking for a specific

disease that may be looking for more general connections or information bio

banks passively collecting disease specific sample samples so this would be bio banks that collect information

incidental to care that otherwise is being provided at the hop so if you go in for a blood pregnancy

test and the blood that is used for the pregnancy test has been retained for

analysis of other things so those

those models are the same in children and adult the last two the last two do

not presently count as human subjects research which makes the informed

consent and reconsent issues for as Lieu but the new rule would arguably

include passive samples which is one of the reasons it's not very popular so if

it does include passive samples and then consent becomes an issue there and

oftentimes passive samples can become a

can require consent if they become be identified in and so in that case you

would be required to obtain to the sent of the participants so so that

recategorize action results that the D identification the re-identification of the samples results in a recategorize

ation of the research into human subject research which requires consent all

right so this is our current common rule in the context of consent for children

and this was just the initial consent so this is not this is not particularly

recent and what this really does is follow the familiar assent permission

format that we see a lot in pediatric care and treatment and uses that also for research it incorporates by

reference provision of the common rule on traditional informed consent as relates to adults in order to obtain the

permission to set the standard for obtaining permission of the parents so the informed consent process for the

parents must include disclosures of pertinent information under Section 116

of the 45 CFR six and the provisions of waiver must

follow that format as well and so briefly for review that the waiver provisions in order to obtain a waiver

for obtaining consent you must have a study that involves minimal risk to the

participant the waiver will not adversely affect the rights of the participant the research could have

practicably be carried out without the waiver and you can talk a little bit about that later and subjects will be

provided a debriefing after their participation or there will be some explanation for why they cannot recently

be provided that debriefing so what's important here in number three is that

this provision is silent on the issue of re consent which is actually you know

kind of a fairly substantial oversight in light of the nature pediatric research in generally so this the

reconsent issue is an issue not just in bio banking but you could imagine that

it might be an issue in other kinds of pediatric research so it is a little

bit of a an oversight so why is we why

we consent an issue in pediatrics by linking it can be an issue in adult bio banking as well but it's important to

look at how pediatric bio banking is distinct from other forms of research

particularly in the adult context and I started for the formatting on this I tried to list the sources at the bottom

so people can read the articles themselves and I think in the transfer up to the big board it's kind of gotten

smooshed but so there are some temporal concerns with pediatric

research yeah pediatric research may take place over a longer period of time

and and it's more likely obviously to bridge the span between adolescence and

adulthood which is the period of time when you would need to reconsider that

there might be physical harm with respect to pediatric research so it's

possible that the information that is obtained as a result of bio banking as a result of

forming those connections between analysis of specimens might result in

changes to clinical practice as to that particular participant each there may be

psychological harm that results from the question of whether or not to provide findings of the research to the

participant economic harm as it relates to the adverse effects on employment if

a participant has a specific diagnosis or condition and the loss of privacy

which is always a issue in any kind of research that the information could be released without consent and there seems

to be a sort of particular concern with that as it relates to bio banking almost

a kind of you know dystopian novel type you know idea that all of your

information is going to be contained in these large computers which would be susceptible to infiltration by you know

whoever and you know where's Tom Clancy when you need him I guess so so these

this issue that so of loss of privacy is a concern for people and so looking at

these general you might think of them as falling really into two categories the first would be the temporal concerns

that brothers raises that has to do with the fact that pediatric research might

be longer term and it's the reasons that issue presents as a result of that

longer term research where it bridges the gap between maybe infancy to adulthood or adolescence to adulthood

these very you know long periods of time important periods of time and then the

other items on this list you know clearly could affect adults too but we

have to keep in mind that when an adult consents to participate in research they personally accept these risks as part of

the potential harm and when a child is involved in research the parent initially accepts these risks on behalf

of the child and even assuming the parent is acting thoughtfully and

morally we could understand that as the child grows they may have different assessment of the risk they

are willing to undertake and reevaluate that as an adult and so we have to ask

ourselves as researchers whether they should be given an opportunity to reevaluate that risk for themselves upon

adulthood and so it is that is the nature of the change in age that makes

the sort of the physical harm a psychological harm the economic harm of privacy issues particularly relevant to

reconsent in Pediatrics by ranking so oh that's too bad so this is I use SOP as

it relates to reconsent so Indiana University has an own SOP specifically

adds to the reconsent issue they have dealt with it affirmatively recognized it as a potential issue and they have guidelines

on this and I'm not going to read them but basically that the IRB could approve

a waiver of Regent sense but that the subject should be given an opportunity

to refit them best year should seek them out and that the research should if the

research does not involve any ongoing interactions or interventions with the subjects but continues to meet the

regulatory definition of human subjects research then it would be necessary for

investigators to seek and obtain the legally effective informed consent of now adult subject so very Pro consent

putting quite a bit of obligation on the part of researchers to get that consent once children become adults it should be

noted that this language is actually the exact language pretty much the exact

language taken from the office for Human Research protections website under their

frequently asked questions section so a

frequently asked question of the office for Human Research protections with how do we handle reconsent

and they have suggested that it followed this format on their frequently asked that have not amended their rule to

formally incorporate this into the common rule so not surprisingly a lot of

bio banks have adopted exactly this language just as IU has and so when you

look to the SOPs of other bio banks other academic bio banks in particular

you will often see what is essentially a sort of cut and paste from from the

frequently asked section site so to the extent that Indiana University is concerned that their policies run afoul

of anything they mean they don't but they do play quite a bit of burden on

the researcher and so we might ask whether there's a way to balance this so

what does it take to reconsent people as adults is it really that hard is it

really that different from problem just a general consent issue that exists in

adult biobank and the result research and I guess I would just submit the answer is yes it is different

basically any research that is going to carry through from any you know under

eighteen age group into adulthood will then necessarily have a two-part consent

process just incorporate it into the research and this makes the consent process of pediatric research more

expensive than adult research and it does have the potential to discourage

overall pediatric research which is particularly true for research that

might involve smaller programs or fewer investigators fewer subjects or a larger

developmental spectrum meaning that if the research involves a number of children who are maybe ages birth

through sixteen or you know something like that where the consent issues might be different along the line so so what

their risk here is is that we might find

ourselves in a situation where we're actually discouraging pediatric research

because we're making it expensive as part of this to consent across

so there are also pragmatic concerns here that are actually probably the

bigger issue so really just being able to get a hold of people once they turn

18 so like getting a call back getting a signed return I kind of feel

like this captures it fairly well that so anybody who is listening who is a

parent of a teenager trying to get a callback from that person if you are not

really their priority so tracking down the purposes can be difficult there is a

kind of progression in research where the more failure to face interaction the researcher has the more involve the

participant in the study the easier it's going to be to get that consent they're still regularly seeing you put the

consent down legal presence at one of their appointments but if the researcher

if the research relationship is more distant to that it can be more difficult so and then even with current contact

information it can be difficult to get a response from an 18 or 19 year old who is out on their own so even if you are

you have a medical record with current and up-to-date information again just

getting that person to respond to be quite difficult and one article I

thought captured as well written by Rush was notice that a two-year follow-up as

part of an epidemiological study demonstrated that a majority of so two-year follow-up a majority of

participants did not respond to mail correspondence and telephone follow-up was resource intensive the allocation of

additional resources required for recon sensing must be considered as these resources could otherwise be diverted to

improving core bio banking operations so the alternative is to think of waivers

in a more permissive way we can have opt-out notification which are which

technically are not consent but for example the Vanderbilt University uses an opt-out format for their bio banking

wares people can sign a form saying don't want their samples to be used in in bio

banking but the rules but and so or we

could think of expanding waivers on a case-by-case basis that includes

considerations of the age of the participant at the time of the initial consent so does it really make sense for

us to be getting a cent and permission when a participant is 16 and then

tracking them down to get their written consent again maybe 18 months later when

they turn 18 that that there maybe we should drop it the age within which we

allow waivers for free consent upon upon

the age of majority so the other questions are going I want to think

about is whether there's even ongoing collection so if you collect and discuss men in the past and you're still doing

research on it and they have implications in a sort of abstract way

but should we really be going back and Rican scenting people if we aren't

really even continuing to collect data from them we're still sort of examining it also issues of EMR

linkages there are ways to you

know see identify the data for the researcher while still allowing the

provider to put information in that the researcher has access to and then this

inquiry of practicability so what's the what where we how are we

going to define practicable if it's different if we want to expand waivers

we might want to look to whether or not we're really being thoughtful and

logical about the cost and the realistic alternatives to to doing that so what a

practice will mean there are there are a few definitions around but I like this

this particular one where something has been practicable if the effort would to

contact the participants would prevent investigators from attaining important research aims and so prevent their

should be read sort of broadly not just literally prevent and then make it

impossible but discourage meaningfully discourage make it considerably more

expensive or have a truly negative impact on the ability to to obtain data

so one of the ways that their rule seems to handle we can handle the

practicability issue with waivers is to suggest that waivers should be rare so they seem to have a quantitative

understanding of waivers that they should not be used very often and then

the new common rule says they should be extremely rare and while it doesn't spell out a sort of audit trigger kind

of framework you can imagine it usually going into that where they really are asking researchers to keep track of how

many waivers they request and receive as a sign of whether or not those waivers

are being handed out judiciously so I

would suggest that the emphasis on quantity is a four metric for whether

waivers are appropriate so waivers should be granted where they are appropriate where research profiles

match the criteria for granting them and some institutions will necessarily have

higher proportions of waivers because of the kind of resources they are doing particularly pediatric bio banking

research so the proportion of waivers or requests and granting of waivers really

should not be factoring into the analogy analysis here and the focus on rare or extremely rare misses the point if there

are criteria for when waivers should be granted and somebody needs the criteria the waiver should be granted so our

takeaways for this for this little chat are that I use standard operating

procedure or reconsent is in line with federal guidelines and Natchez a frequently asked question cite the way they've got

it set up is perfectly acceptable but the federal guidelines themselves not

absolutely address issue we need to pediatric bio banking and the emphasis

on rarity of waivers misses the point we should be refocusing refocusing on the

appropriateness of waivers the practicability of reconsent and whether or not it will be

detrimental to establish meaningful research out when you're out static I

will open the floor to our in-person representative think some of you have

heard on our taping we've got a tape but if you're if you're live with us before

we started today were chatting about a few things including hopefully by the next talk I have a personal a better

picture of the speaker's face because I think our pictures now from the end of the room and more importantly an

opportunity for people who are watching so they'll call it and ask questions or maybe even send in questions when we

post this also will will look for an opportunity filters and in comments questions we can respond to through the

be SAP program so they may questions

here I mean I'm looking directly at Marriott was our local expert on this

topic before we got involved in this particular round and temp she's involved in this investigation we've we've been

underway and in a thoughts or questions Mary thanks a lot you know it's very

interesting

into what we ought methanol guidance

around the begin one of the limits of crafted facility what's allowed under

practicability you know it's something like this perfect Turner where everybody sort of knows

what it means that no one can put a perfect death there was a clear definition to it I don't know if you

could tell us you're thinking about like how like should we I you I Rd Coby going forward in terms of assessing plastic

ability what would make things practicable and where would you put limits on it well I think I think

there's a tendency for people to confuse practicability with impossibility and so

we don't want to be suggesting that the standard for researchers would be that they don't have to obtain reconsent or

in order to avoid obtaining reconsent they have to prove it it would be impossible to do it i guess a sort of

five-year-old term effects ability would be really really really hard which the

intent of that claim can be but it's just really hard yes there's an year-old

use the same texture but I think it's also you know we can we can look I don't

want to you know rely on cliches or whatever but it does tend to be I would think for legally from the IRB

standpoint of like you know you know what when you see it that whether the person is really trying to skirt around

the the waiver issue by suggesting that you know it's going to be really hard

because our copiers down versus somebody who's saying I have 15,000 participants

in this study I got all of their consent you know two years ago when they were 14

15 and 16 years old and you want me to go through that entire same process now we will you know increase the cost of my

research outside of the budget for the research I have to cut the same sighs in half that sort of thing can you

go back to the slide on waivers that was a great slide and by the way dislodged from hard to read right now people

watching will probably I'm at a curio Claire yeah PDF physiology where is it

forward forward forward here dispute appear yeah so the waiver is essentially

you know the impacted ability I think the history of not X grounds Eric used to talk about our farmer directors of

visa program and of the Center for Bioethics who was basically around at the you know HHS when they were coming

up with practicability I believe in shortly after the comeuppance idea as I

formulated some these regulations and you know he emphasized in that reminiscence that that it had been you

know a term that they needed a concept of this like really difficult because they couldn't require as

impossible but in since we are luxury being the ethics people assisting you know the impact ability excuse is

only available if there are not any you know important violations of people's rights or putting people away at harm

and so you might say well as long as there aren't such violations of people's rights or harms Why should there be any

standards and within a low standard sort of appropriate given we've already included the requirement that there's a

minimal risk to the participant right the waiver will not adversely affect the rights of the participant in a research

and but practicability is actually part of those prongs and that's tremendous light yeah that's okay I'm just thinking

this through that you know I guess it's almost up I can't really describe it in words but it's almost an inverse

relationship as the danger and harm participants goes up the standard reflects ability could go up pretty fact

ability could go up advocates in the regulations but it's almost if you think through this ethically the excuse saying

really I can't do this please let me do this research even though I can't do this people back maybe three content

it's important enough and it's going to be bad you're limited harm to my participants in the scientific outcomes

report of whether that is interested third factor which is not I guess in here which is how important research yeah which is again very very

hard to assess right basis everybody thinks the research is very for you do we do the other thing I think that's

interesting and I didn't include in here but probably should have is that a lot of the things that you would think of as

being that a lot of the things that makes reconsent sort of silly so you

know if you consented somebody at 16 or 17 and you think they're relatively mature and you should not have to go

through the whole process again just because it turned 18 that that profile of the maturity of the participant and

the sort of psychological that stuff is part of the initial consent consideration so a painting they're up

sent to their research that brings with it containing their and so if they pass that first threshold of being sub a that

has a responsibility to assent in the research then revisiting it makes even

less sense after age 18 fascinating I'll

say in terms of the take-home point we do think of multiple audiences for this because some people certainly watch this now or the future who have a morbid

ethics background who may have enjoyed our past ability discussion there and assume that's a continuing area of

interest for the VFC program and Center for Bioethics especially as we think about biotech research and other

verities of precision health research but for people who are researchers I guess who are just designing a biobank

involving pediatric subjects maybe another way I would summarize your point may be overly simply is these are the

regulations you have to abide by them but if did we consent will be incredibly

burdensome yeah think about applying for a waiver yeah releases of Sandow waivers are a

place to go to make that case and the IRB has the freedom to now if this is

recorded and and played later after this left to take it off the web if the new common rule comes through with sniffing

changes in this will put an addendum on or maybe to talk again with the new common room I'm pretty against those

working on the background and regulation or ethic to listen to this talk there's a common rule changes that are being

considered at this point it looks like I guess as time passes we may not see it

pass before the the administration and so we may or may not see these David which is pretty good

and bad I mean that we miss an opportunity with the new rule to include a reason that provision that's workable

although how much space do we have that there reconsent provision would be workable based on what it is proposed

now not a lot you know on the practicability issue the other code that

I would throw out for investigators would be thinking about whether the

reconsent changes you could imagine that if you're

doing research on a sensitive topic I had a colleague who did research with adolescent fertility preservation and

oncology you know and you know you could imagine that you know that that at

reconsent there may be some issues you may be there certain types of people that we may be more or less likely to

retain events so there might be types of participants some participants are more

difficult to find there would be biases it is particularly families lower-income

families they have be more difficult to track because they have more frequent rooms there so you may think about how

ill the participants are the first time they were consenting to take as well as 1517 it should be able to consent if

it's an oncology diabetic in their conservative diagnosis and they're very

sick it may be it may be or may be better just reconsent them after they're better they don't I mean I get may not

be the 18 rule but there may be sort of how that how content is done in the

first place does it change are there going to be biases in terms of whose baby you're able to maintain in the sample you know

the types of ongoing access with you you know sort of you know wonder they download and link it to the EMR so it

feels like there's sort of pieces to it that may be relevant to this

like how practical is it in addition to cost and burden well and their reconsent

issue to become the problem if we require a reagent scent and can't yet I

mean if we're really sort of proponent about it you have you have to continue then what is really the requirement for

how the sample is handed or the information or the data is handled if you can't get it which I didn't even

include says it's such a messy conversation with and do you have to hold that data out of your study the

data you've acquired up to that point that the rule as it exists actually says

we suggest you don't but I mean you know what are you doing in in those

situations where you might have somebody who says no I don't where you consent and I don't want my information being

used as part of this research study pretty good like maybe an individual resource research where somebody says

you know I'm thrilled that you've done its Marshall study to see whether kids Hooten you know not eat the marshmallow

will be high functioning adults but I don't want people to know that I was a kid who ate a Marshall 450 being white

about it but there's obviously more significant research than that I love the marshmallow thanks study and

we are sorry to tease those who are listening who don't know I don't know what your Google Google of radio lab

which recent did a show which I've nothing about that about it's ready a lab on a topic of fate and what baked

means and whether you can identify individual state identifying that love self control such as myself okay so um

so why I want to I want to all states a little broader so as we think about the

reconsent issue as you correct I think really well point on this talk to really appreciate I think we all should appreciate it and learn from that this

is related to the question of consent or biobank studies and of course a debate

we've been going on for a long time over whether blanket consents of a one-time consent it ever appropriate in a biobank

and I think my sense of the literature and the practice is that it is generally accepted now which in leaves sort of as

a last sort of a last lingering question whether as leaves the transition from pediatric to adult hood would be a

reason for Rican scenting if we're giving up on Rican scenting in many cases adults who consented once do you

think thoughts on that sort of how that I need a link to those debates you get to you get to kind of the layers there

and the layers of issues so a blanket consent you can imagine makes sense for

research that might change or samples that might be used for more than one kind of research and and so adding the

the vulnerable population of a child to that it does make it slightly more

difficult in that many adults when they sign up like a blanket consent cannot

even conceive of all of the different ways in which that sample could be used for research and so then you have an

adult consenting them you have a child so it's just the layer that it does make

it more difficult is pro pro research as i said to you guys before that i think

we should be looking for ways that we can definitely facilitate research not ways that we can identify ethical problems and share research down so but

certainly the layers the more layers you have of analysis and no tissue there the

more complicated I wonder if with this talk what if we could do that what if we could also put

up probably not at the same time but the literature on actual harms to people

participating in by a bank research I wonder what is there in terms of whether there are any documented cases of

individual harm from his bidding of biobank now you can say there dignitary arms always independent of any provable

or recognized direct arms so the harm of

having a research done now I suppose them the great court cases around his

bio Bank Reacher's research doesn't let his super I tribe I guess successfully brought a complaint over the use of

their data in a way that was really a signatory say it's probably worth looking into and

for those who would make a claim about maybe a request for a waiver maybe we

should make some of this harm literature if there was any available we could talk about that I shouldn't make work for

ourselves but it's an exciting area but maybe we're getting close to the end e about theta is the but B step program is

trying very hard as as IU moves into this precision health initiative now and

I am some aggressive and innovative attempts to construct cohorts and and to

expand biobank research here really getting clear on what is known and may

be from the cutting edge I think issues here is probably a good idea for us to do so I like that sir is next up okay so I

guess that's it unless Tom do you have anything I didn't put you on the spot because you're a graduate student so you get away with anonymity if you'd like

anything else Mary India yeah we're good okay we're

all good so thanks a lot Jane and we'll go ahead and wrap it up again actually those who are listening before we even

post this if you have questions you can get to ask as we do not activate that functionality specifically to email me

or Jane or the beset program all available on the web so Peter Schwartz at the IU Center for Bioethics Jane

Hartsock you can contact us through the IU Center for Bioethics or work through IUPUI and have a great day thank you

very much sure