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IN THE CIRCUIT COURT OF THE TWENTIETH JUDICIAL CIRCUIT

ST. CLAIR COUNTY, ILLINOIS

FRANCES E. KEMNER, et al.,	)	
	)	
Plaintiffs,	)	
	)	
vs.	)	No. 80-L-970
	)	
MONSANTO COMPANY, et al.,	)	
	)	
Defendants.	)	

REPORT OF PROCEEDINGS

APRIL 13, 1984

Before the HONORABLE RICHARD P. GOLDENHERSH, Circuit Judge

APPEARANCES:

MR. REX CARR and MR. JEROME SEIGFREID, Attorneys at Law,
On Behalf of the Plaintiffs;

MR. KENNETH R. HEINEMAN and MS. JANE RUDOLPH,
Attorneys at Law,
On Behalf of Defendant Monsanto Company; and

MR. ALBERT SCHOENBECK and MR. STEPHEN SCHOENBECK
Attorneys at Law,
On Behalf of Defendant Norfolk & Western.

KAREN D. HOPKINS, C.S.R.

OFFICIAL COURT REPORTER

BE IT REMEMBERED AND CERTIFIED, that heretofore, on to-wit: April 13, 1984, the matter as hereinbefore set forth came on for hearing before the Honorable Richard P. Goldenhersh, Circuit Judge in and for the Twentieth Judicial Circuit, and the following was had of record, to-wit:

THE COURT: Good morning.

(Direct Examination of Dr. Ellen Silvergeld continues by Mr. Carr as follows:)

MR. CARR: Dr. Silvergeld, can you see that?

DR. SILVERGELD: Yes.

MR. CARR: Can you?

DR. SILVERGELD: Well, I can--

(Plaintiffs' Exhibit No. 235 was marked for identification by the court reporter.)

Q (Mr. Carr) Showing you what has been Plaintiffs' Exhibit No. 235. Could you tell us, please, what that is? You can use a pointer if you like.

A Thank you. This is a systemic representation how heme synthesis, porphyrin synthesis takes place inside a cell. The cell that's shown here is a liver cell, but this

is really similar for all cells. Nerve cells, kidney cells, any cell in which this pathway, this metabolic pathway exists. And what it indicates is how well-controlled this system is. That is, the purpose of this metabolic pathway of this biochemical factory, if you will, is to make heme. Heme is a very important molecule for incorporating into the red cell, the hemoglobin, to carry oxygen, but it's also a very important molecule in many kinds of other enzymes, including those enzymes that dioxin induces, those arylhydrocarbic hydroxylase enzymes. It is also very important inside cells as in red blood cells for providing the basis for carrying oxygen. It is really the molecule which in humans and mammals carries oxygen. And the very similar kind of molecule, chlorophyll, performs that same function in plants. And just as our oxygen molecule, which is known as a pigment, is brown, which you know if your blood comes out of your body and dries it turns brown, that's because of the heme. The oxygen carrying pigment in plants as you know is green, that's why they are green. But it's the same system. But what this shows is the various steps at which changes tu rn on or turn on the system. It's a very well-regulated system, and you can imagine why. This is absolutely the critical molecule for our bodies to have. Without it there would be no oxygen delivery in the lungs, in the blood, or within the

cells and we would instantly die.

Q Heme is then kind of like a little truck or car that's carrying oxygen from the lungs to the various parts of the body that need that oxygen?

A That's right. And anything that decreases heme or changes it has very serious effects on the body. For example, the disease known as sickle cell anemia is a hereditary disease in which this molecule, the red blood cell, is deformed. It has an abnormal shape, and one of the consequences of that abnormality is that it doesn't bind and carry oxygen quite as well. And that's why people who have sickle cell disease have what is called crisis. And the crisis is a failure of oxygen to get to the cells where it is needed. When there is a very great decrease in this compound in the red cells, you have a condition known as anemia, which in terms of language just means lack of heme and hemia. But there can be other consequences of a decrease of heme which we have talked about, and that is if you don't have enough heme to support other metabolic pathways, then the body's ability to deal with sex hormones, to deal with drugs, to deal with a variety of other compounds, including dioxin itself, becomes inhibited. What this shows is another way of looking at what we looked at before, yesterday, in really an arranged sense, and that is that when dioxin,

2,3,7,8-TCDD, or in dechlorinated phenols and many other compounds come into the body, one of the things they do is put a big demand on heme. That's because their own metabolism requires heme. The enzymes that break down dioxin are heme-contained enzymes to get a demand, a drain on this heme pool. One of the consequences of that is that up here the level of the gene there is a message sent back which says make more heme, I need a lot of heme, says the cell, because I've got to take care of this dioxin which is coming to my body. So operating through this genetic structure, what are known as regulatory genes, operating genes--

Q Is that APO, that drawing for the APO stands for gene?

A That's an APO heme protein, and this is thought to be the molecule which actually interacts at the level of the regulatory gene and turns on an operator. Actually, if you will, going back to our analogy, dials the telephone and talks to this message. And here is the actual message, messenger RNA, which goes back down into the mitochondrion. That's what this is. This is the nucleus. This is the mitochondrion of the cell.

Q Now, hold it a minute. The nucleus, the mitochondrion, what is that, the covering of the cell?

A No. Mitochondrion, they are all inside the cell

here. Here is the boundary of the cell. It actually goes up here, as we cut the nucleus in half on this picture. Another part of the cell, which is a self-contained little unit, is known as the mitochondrion, and one of the many things that the mitochondrion does is transform oxygen into energy. That's why it has a lot of heme in it, and it is also the place where heme is made. So when this message goes back up to the nucleus, the nucleus through its genetic machinery, calls back down to the mitochondrion through this messenger, RNA, which is really what the name says, it's a messenger, it's carrying a message from the gene down to the mitochondrion again and says we need more heme, make some more. So this message goes back into this little factory, if you will. The mitochondrion is basically a major energy factory for the cell. And what this message is is to talk to this enzyme, and it says make us some more heme. This is the enzyme, ALA synthetase, which controls how much heme is made in the body. And when this enzyme is turned on or induced, then you get more of the first precursor for heme and this increased amount of ALA, amino levulinic acid, which is the first molecule which enters into this pathway.

Q By that you mean the first step in making heme?

A The first what is called committed step. These molecules glycine and succinyl-CoA, which are taken by ALA

synthetase and made into ALA. These go off into a variety of other things, but this is what's called a committed step. When you make ALA, which you are going to be doing, the mitochondrion makes ALA for you, is to go through this pathway and wind up with heme.

Q And when you get down here this PBG stands for what?

A That's porphobilinogen, and this is the first of the porphyrin-type molecules. One of the interesting things about this pathway, as you can see its got a lot of areas where it talks to itself. It says make me more, make me less, stay just in the right range. The other thing that it does is it works inside this mitochondrion and outside. And that's one way it also regulates itself. So this is one reason why in some of the porphyrias, the diseases which are disorders of the system, the system can get out of control, because if something happens out here, this is out in the cell, the mitochondrion doesn't know it. It's happening away from the mitochondrion, and that's why you see in some of these acquired or chemical porphyrias these very specific derangements in the level of these intermediate porphyrin compounds going from uroporphyrinogen to coproporphyrinogen, because they can't be regulated or shut down up here because the inside of the mitochondrion doesn't know what's going on outside in the cell.

Q And in the laboratory then it indicates that there are abnormal amounts of these porphyrins and the intermediates being excreted?

A That's right.

Q That's a sign that something is going wrong with the mitochondrion and the messages?

A It's a sign that something has gone wrong with this system, but more than that it can be used as a very specific sign, because you can see this is a fairly implicated metabolic pathway.

Q Yes, that's what I can see.

A On this figure we have even left out several of the steps that go on in here. To go from porphobilinogen to coprobilinogen is actually about nine steps, but fortunately they are not all on this graph, and changes at any point here or up in here are quite characteristic of the kind of the porphyria you have got and also to a certain extent the kind of chemical exposure you might have had if it's a chemical porphyria. For instance, lead has a very specific effect to block this enzyme. So with lead poisonings you don't see too much an accumulation of this molecule, but you see an awful lot of ALA, because the enzyme which is going to take ALA and make it into porphobilinogen is blocked and you see that increase. Now, with the chemical porphyrias such as those associated with 2,3,7,8-TCDD,

but the major effect is here to switch on this whole system, what you see is a great increase here and also some very characteristic patterns within here, because dioxin also has an effect on some of these enzymes, these uroporphobilinogen decarboxylases. That's what UROD stands for. And what they do is a series of them, three or four of them, which take uroporphyrinogen and make it into coproporphyrinogen, and that's a stepwise process. You can't skip over it. You have to go in sequence and there are several enzymes involved. And in addition to its effect here, dioxin has some effect down here. So by looking at the pattern of these porphyrinogens as well as the whole system of its productivity you can make some very good scientific deductions about the kind of thing you were exposed to and what the implications are for cell function.

Q Is that about it with this exhibit, Doctor?

A I think so.

Q Thank you.

(Plaintiffs' Exhibit No. 236 was marked for identification by the court reporter.)

Q Now Doctor, Plaintiffs' Exhibit 236. Does it deal with the very subject that the other chart dealt with that you have just discussed?

A This is a very similar picture. It gives you a little bit more of a sense, I think, of how this factory works and how it talks to each other at various steps. It doesn't give you an idea of where these things are occurring. I think the advantage of the other figure is that it showed you where some things were going on inside the mitochondrion and other things are going on outside, and it helps us to understand why things can get out of wack, because parts of the cell can't see what's happening in other parts of the cell.

Q Now, over here at the left, Doctor, it starts with succinyl and glycine. That I take it is the raw product that ultimately when the body does certain things that it's going to end up in heme and--

A Right. These are small amino acids, glycine and succinyl-CoA, and these are used in many parts of body metabolism. One of the things they are used for is they are put together by this enzyme, ALA synthetase, and made into ALA. And as you see right there, this is where you enter the hepatic synthesis of porphyrin--

Q Doctor, when we say succinyl and glycine, in what foods or from what foods does the body make or derive succinyl and glycine, or does it do it from all foods?

A No, not from all foods. Succinate and glycine are compounds that are taken in in our diet and they are important

to us to eat. They are found in many vegetables and in meats and meat derived products.

Q But these are elements or things that are found in the food that we eat?

A That's right. These are building blocks of our body's chemistry.

Q And the body-- By the time it's succinyl and glycine it's already gone through various stages and steps in the body in the digestive and transformation system?

A Yes. Succinate is a product from sugar metabolism and a range of other basic metabolic processes. Glycine you mostly get through diet. We are dependent on our diet to get glycine. There is a step at which succinate is bonded with co-enzyme A, that's what CoA is, which makes it active, biologically active. And these two relatively simple molecules go on and enter the metabolism.

Q Now, the ALAS with the arrow.

A That's an enzyme.

Q That is an enzyme. All right.

And that enzyme then turns into a porphyrin precursor?

A It makes the porphyrin precursor out of these two materials.

Q All right. And that's the enzyme ALA plus the porphobilinogen?

A No, the enzyme is ALAS. What it makes, I guess an analogy is to think of making a cake and if you mix flour and water and eggs and baking powder and everything else together, those would be here, those are your ingredients. You put them in the oven and you turn on the heat. The enzymes in the oven, without the heat it doesn't become the cake. Without it you don't get the cake. What you get is here are the cakes or cakes and cookies, ALA is your cake. Then you do further things by other enzymes and that becomes PBG.

Q All right. And then that porphobilinogen goes into that arrow, that's uros, uropos.

A These are two more sets of enzymes. Uro synthetase and uro cosynthetase, which appear to act together in a very complex way and produce the first of the porphyrinogens, as they are known, and that is uroporphyrinogen.

Q Now, I don't see in that stage there that which was previously known from our Exhibit A in the Ellefson Deposition, heptacarboxylic and hexacarboxylic and pentacarboxylic. Are those intermediate steps in there but not on the chart?

A That's right. Those are all molecules from here to here. They are not shown here, but there is a series, as I mentioned in the last exhibit, of enzymes which are known as urodecarboxylases, which start with this molecule and eventually wind up with this one, and they go in a very precise stepwise

fashion. And what they do, they are called urodecarboxylase, and although that name sounds bad, it really says exactly what it is. They strip off a carboxyl group. They de-carboxylase.

Q Well, that doesn't help us unless we know what carboxyl is, which I don't know. What is a carboxyl?

A Okay. Carboxyl is carbon oxygen groups, set of atoms, which is attached to the porphyrinogen molecule, and in order to get down here you have got to get rid of some of those carboxyl groups. They are not what you want in order to make heme. And so this set of enzymes takes one carboxyl off, start with seven, hepta. Remove one carboxyl by decarboxylase and you get hexa, that's six carbons. You take another one off by another decarboxylase you get five, that's penta. You take another one off and you suddenly get coproporphyrinogen. But these are a set of specific enzymes, and you can't go, you can't jump, you can't go from a seven carboxyl down to a four without going all the way through the process. And as I mentioned, 2,3,7,8-TCDD has some independent effects on this family of enzymes in addition to its effects to drain this heme pool.

Q So actually in this diagram TCDD would be acting in two places, acting on the heme and acting on the porphyrin intermediates?

A That's right.

Q All right.

A It would be acting there.

And the next stage is to take this molecule, and by an enzyme known as coproporphyrinogen oxydase, that's what the O stands for, you turn it into this molecule, protoporphyrinogen. Proto just means near to the protoporphyrin. And by another oxidase, that is another enzyme which is going to add an oxygen. Actually enzyme names are pretty logical. Oxydase means it's adding an oxygen. Decarboxylase means it's taking away a carboxyl. Hydroxylase means it is adding--

Q Doctor, not to argue with you, it's logical to you if you know all those words to start with, but if you don't know them it's not logical. It makes no sense at all.

Now, we were down to the protoporphyrin. Where do we go from there? What happens there?

A All right. Now, you have the basic heme molecule, this protoporphyrin 9, as it is known, and you can even find this molecule in your blood, because what makes this molecule different from heme is iron, and that's why heme is brown, because it has iron in it. Iron is what makes it able to bond oxygen. And so ferrochelatase is the enzyme which puts iron into protoporphyrin to make heme.

Q Again another enzyme doing that?

A That's right. If you were an oyster it would put copper in there, but it would be exactly the same process.

Q If I was an oyster it would put copper in there? Doctor, let's get back to the chart.

All right. What is it doing now? This enzyme is putting iron and we are ending up with heme?

A That's right.

Now, you have the molecule which is all put together in terms of its structure. It is very stable, a very beautiful molecule, and it has iron in it and it is ready to bind oxygen. So this molecule is taken away and put into various proteins such as hemoglobin. It combines with a globin molecule, which is in your blood.

Q All right, Doctor. Bring this chart back for a moment. We are on this APO, APO-protein thing. We are right here now?

A No.

Q No? I thought I had something.

A No.

Q Go ahead, Doctor.

A Okay. What has been realized now, and that's what is shown here as well, is that a lot of this heme is being taken away by the body and used in all those enzymes and in the blood and in all the other places where you body needs

heme, but there is a little bit of it left over, and that is used to send a message back to the nucleus to let the nucleus know whether it's going to switch on the system again. Shows a little bit better here, and that is known as the free heme.

Q All right. This free heme, then, is what's going from here to here?

A That's right.

Q Sending that message?

A That's right.

Q Well, see, it was.

A Right. Obviously the cell, liver cell or whatever it is, doesn't communicate with your blood cells, so the liver cell doesn't know if you have got anemia, a lack of heme in your blood cell. The only thing it knows is what's going on inside it, because every cell is a little world of its own surrounded by this fat or lipid wall, and so the system sets up a little bit aside to let the cell know itself whether something is wrong and it needs to make more, most of which will go outside the cell into other functions, but a little bit will stay. It would be as if you had a savings account and you wanted to keep track of how you were doing with your money, so you set a little bit aside on top of your dresser and every time you took $10 out of your savings account you took 10 cents off your dresser, and when you got down to

30 cents on your dresser you knew you were in bad shape in your savings account, so you put some money in your savings account. That's what this regulatory pool really is.

Q Does TCDD interfere with that free heme as well?

A That's what it appears to do. It sweeps right through here and takes them out.

Q Now Doctor, how can scientists tell or how have they discovered that 2,3,7,8-TCDD does interfere in these processes as you have described? How did you all discover that?

A Primarily through experiments on animals, but also because through studies on people exposed to these chemicals there was evidence that some of these end products were altered. We also knew because of the literature which had been developed on other diseases of this pathway, other porphyrias. But its been primarily through a research on animals that understanding has been gained of this entire system. Now, most of this knowledge has also been shown in liver cells taken from humans and skin cells and red blood cells which have an awful lot of this same pathway.

Q Doctor, I covered up biopigment. What has that got to do with the processes?

A Well, these are bilirubin and other kinds of things which show up in your bile and another indication or another way in which this system takes care of itself. If through

some chance there is too much heme being made, or, and this happens with lead poisoning where you get this tremendous reduction, then this enzyme switches on, which is known as oxygenase, and what it does is degrade heme and then allows your body to excrete it and get rid of it.

Q Now, can you detect in animals and in humans possible effects of TCDD by measuring or analyzing the bilirubin?

A That would be an index of an alteration in the system, yes. Bilirubin is commonly monitored, and indeed there are medical conditions frequently found in newborn children known as hyperbilirubinemia, which are quite dangerous.

Q And can or does TCDD have a role to play in that?

A Yes, it can.

Q Anything else on this chart, Doctor?

A No, I don't think so.

(Plaintiffs' Exhibit No. 237 was marked for identification by the court reporter.)

Q Dr. Silvergeld, placing now on the stand what has been marked Plaintiffs' Exhibit 237. Could you tell us, if you would, what that chart shows us?

A This is a chart taken from a study of the effects of 2,3,7,8-TCDD on guinea pigs, as you can see, and what it is is

an attempt to understand why exposure to 2,3,7,8-TCDD causes a very great hyperlipidemia, that is a great increase in fats in the blood. Now, as I mentioned, one of the other things that TCDD does is to supress appetite, and in certain animals this suppression of appetite can be so extreme that the animal begins really to waste away. And in the process of reducing food intake, as those of us who have tried to diet know, you hopefully are burning up lipids or fat in your body. So just by reducing your food intake you could have hyperlipidemia, that is an increase of fats in the blood. So this experiment is trying to determine whether there was a direct important effect of dioxin on lipid metabolism which would lead to this blood condition or was it all due to a decrease in food intake. And the way they did this was to run different kinds of groups of animals. First off there were animals that were exposed to 2,3,7,8-TCDD and allowed to eat as much as they wanted to eat.

Q They were exposed to the TCDD, they weren't fed TCDD?

A They were fed TCDD I think for a couple of weeks, and a relatively small amount. I would have to check the paper to give you the amount, but certainly well below a lethal dose in this species.

Q All right.

A Now, these are controlled guinea pigs who were

treated just the same as the dioxin guinea pigs also allowed to eat as much as they wanted and then looked at for blood fats.

Q When you say control groups, what do you mean by control group?

A A control group in an experiment is a group of animals that's treated just as similarly as possible to an exposed group here, a group that's been treated with TCDD, except that they don't get TCDD.

Q And in testing of humans, are there also control groups for certain types of laboratory analysis?

A It's very hard to have control groups for humans, of course, because we can't make sure that all the conditions are the same, but there are in general what we consider to be normal or healthy groups of people who are used as standards by which we compare.

Q And so when you talk about a control group here in the animal, you are actually talking about a standard or a normal so to speak?

A That's right. This could be called a normal group.

Q All right.

A But you will see there are several control groups, and I will get to that.

Q All right.

A But these animals are very similar. They are

allowed to eat as much as they want, but remember the dioxin animals are not eating very much.

Q They are not eating very much? Why not?

A Because one of the effects of dioxin is to suppress appetite.

Q Uh huh.

A So when they are left alone, given as much food and water as they want, they just don't eat very much. If you take control animals, normal animals, they will, of course, eat and drink normally. Now, if you look at these levels, the levels of cholesterol in the controls are 27 and the levels in dioxin animals are 130. Very big increase.

Q Doctor, you said cholesterol, but I don't see that on the-- Is that--

A Cholesteryl esters, yes.

Q That--

A That includes cholesterol.

Q Is that another name for cholesterol?

A It includes it.

If you look at triglycerides, which is something commonly measured in human blood, too, it's about 54 in the normal animals and its been increased by about three times to about 150 in the dioxin animals.

Q Now by that, when the dioxin animal, when its blood

was tested it was found to have three times the amount of triglycerides that the control or normal animal had, is that correct?

A That's right.

Q And the only thing different between those two animals were the fact that the one with the 53 parts of triglycerides was not fed dioxin, whereas the one with nearly 150 triglyceride was fed dioxin?

A That's right.

Q All right.

A Now, if you move to another major group of fats which are measured in blood, these are the phospholipids, that is a fat that has a phosphate group on it. It's just a different type of fat. You see that in the controls, the normal animals have about 21 milligrams per hundred, ml, and that's about more than doubled in the dioxin-fed. If you move down to free fatty acids, which is also frequently measured in people as an index of abnormal body chemistry, in the control, normal animals about 18, and it's nearly doubled in the dioxin-treated animals.

Well, this experiment went further. As I mentioned, these dioxin animals are not eating very much, because of other effects of dioxin, possibly on the brain. There is a center in the brain which controls appetite, and this is data

indicating that dioxin affects that center. So they tried to get at this problem by taking two other groups of animals. Now, these animals were not exposed to dioxin, but they tried to make these animals behave like the dioxin animals first by only allowing this group to eat as much as the dioxin animals were eating. The way you do this is you weigh out food and put it in a cage with the animal and you measure how much the animal ate in one day. Let's say the animal ate 12 grams of rat chow or guinea pig chow. Then you say okay controls, that's all you're going to get the next day. That's what's called pair feeding. So they only get as much as the dioxin animals were going to eat. What you see is even if you do that, the levels of plasma fats are much lower in the control animals, even with the restricted diet than they are in the dioxin-treated animals. So it had nothing to do with food intake. It wasn't because the dioxin animals were less hungry, because they had this tremendous elevation in fats in the blood.

Q All right. Now, if those fats in the blood were there, and apparently this indicates they were there, independently of the amount of food that was taken in, if I understand that correctly, where did that cholesterol, those triglycerides and phospholipids and free fatty acids come from in the animals that were given TCDD if it did not come

from the food?

A It must have come from abnormalities in lipid metabolism in the liver. What this is, say that there is an effect of dioxin on the metabolism of fats in the body which is over and beyond what is happening in terms of the animal's intake of fats. And this would indicate that for humans as well. It is not because of changes in diet, but there is an increase in blood lipids, but it is really because of the dioxin. And they just did one other maneuver here to make sure of that. They said let's not pay any attention to how much these animals are eating, let's match them on weight. These dioxin-treated animals are going to lose weight because they don't eat and possibly some other reasons as well. So they took some animals not treated with dioxin and made them lose weight down to the level of the dioxin animals. As I mentioned to you, if you lose weight, one thing that happens is as you burn up fat that fat goes through your blood. So that does, can elevate levels of lipids in your blood. And again, they found that by reducing the weight of these animals by the weight of the dioxin animals, that still didn't cause an increase in lipids. So once again the evidence shows that what's causing this hyperlipidemia in the animals is 2,3,7,8-TCDD.

Q And Doctor, when you talk about this cholesterol in

the blood, the TCDD animal, is that the same cholesterol that's associated with heart trouble, heart disease in human beings?

A Yes, it is.

Q And there is something then in TCDD that causes the body to manufacture more cholesterol and more triglyceride and more phospholipids and more free fatty acid than the body would ordinarily have even with normal eatings, stringent eating, or fasting or whatever?

A That's right. There is something either in making too much of this or in not metabolizing.

Q Anything else on that?

A No.

Q Now Doctor, is there such a thing in experimenting with these animals and in real life with human beings as a level at which a toxic or a drug or a chemical or a toxic substance will have no effect upon that animal or that human being?

A Yes, there can be.

Q And are the words or the phrase no effect level something that is used with reference to discussing the toxicity or the prospect of harmful effects from various drugs and toxic substances?

A Yes,

Q Now, does dioxin, that is, 2,3,7,8-TCDD, has there been yet established by the scientific community or by anyone responsible for establishing such levels, has there been a no effect level established for 2,3,7,8-TCDD?

A In most of the effects of dioxin the answer is no. And if I can draw you a little picture maybe I can explain why this is.

Now, a no effect level, which is sometimes called a threshold, it looks like this. This is what it means. After you do an experiment with a drug or a chemical, you construct a little graph, and on that graph you look at the dose that you gave the animal and you look at the effect you measured. Now, you assume, of course, that the more of a chemical or the drug you give an animal the greater the affects is going to be. But the real question is whether there is a range of doses, low doses at which there is no effect, nothing happens to the animal other than the way the animal normally is, so that the levels of triglycerides don't go up, numbers of spontaneous abortions doesn't increase, rate of tumors in animals doesn't change, whatever it is, nothing happens until you reach a certain dose and then you start to see an increase. Now, this would be called, then, a threshold or a no effect level.

Q Now, has there been no effect levels established for

wide variety of drugs and chemicals and substances?

A For certain chemicals and for certain effects, yes.

Q Why does one, and if I am understanding correctly, that means you can give this amount or a particular amount up to a particular amount and the human body or the animal body in all of its respects it will have--that dose will have no effect that you can demonstrate at least or you can discover or see. That dose will have no effect on that animal, is that correct?

A That's what that means, but there is--

Q All right. Why are no effect levels established for certain of these chemicals and drugs? What's the purpose of it?

A The purpose is to give a range of doses or exposures where we can feel relatively safe. For a drug, of course, it's to give you the point of a minimally effective dose if you are trying to treat a disease that if you don't give at least that much you are not going to have an impact on that disease. But the really important thing to keep in mind whenever anybody talks about a no effect level is first, what is the effect and how carefully did they look. If you are, for example with dioxin, looking at an effect on the liver. And for nearly 12 or 13 years experimental toxicologists have been looking at the effects of dioxin on the liver. Now, the first ways in which

that was studied was really to open up the animal and look at the liver. And if it was all chewed up, if it looked very yellow, it was hemorrhagic, that is if it had blood in it, it was clearly damaged, but that is obviously a very crude way of looking at the liver. But under those relatively insensitive ways of looking at the liver, people propose that there was a no observed effect level of the liver and TCDD. However, many other scientists have gone back knowing what we now know about the liver and how to look at it in a more sophisticated way and we now know the effect of one of these enzymes, that's what causes hyperlipidemia, so what you really want to look at is that enzyme and not necessarily wait until you can measure the lipids with a much more sensitive look. And the most sensitive look that I know of has been done by Dr. Kaminsky and his colleagues at the New York State Department of Health, and he has not been able to find a threshold. There is no threshold. There is no dose that doesn't cause an effect on the liver in the experiments that Dr. Kaminsky has done.

Q Doctor, does that mean that he has given the very smallest possible dose that he can devise a way of giving a dose that small, the very least amount possible to give of TCDD to these experimental animals and he has not been able to yet give a dose so small, no matter how infinitesimally

small it might be, that doesn't have some effect on the liver of that animal?

A That's right. There is no dose that he has given, no matter how small, and he has given very, very small doses, that he did not find an effect on the liver. And these weren't trivial effects. These were effects on the shape and normal appearance of cells as well as effects on some of these enzymes we have been talking about.

Q Now, what other organs or systems in animals and humans have they looked at to determine whether or not there are or is a no effect level in those organs, in those systems?

A The other system which was looked at in this way was on reproduction. And again, it was claimed early in the looks that people have been giving at dioxin that there might be a threshold or level of doses in which you didn't get an effect on reproduction. Now, what were they looking at? They were looking at the failure of the mother to give birth to live animals. That is, the rate of abortions, miscarriages, and of fetal death, the death of the fetus before it was born, and of major birth defects, such as cleft palate and the other kinds of things we talked about. Again, they started to look, and this work was done by Courtney and Moore and others, began to look more closely at reproduction. Look, for example, at the weight of the animal when it was born. And we all know

that birth weight is a very important thing in reproduction. It has a lot to do with the future success and development of children. Began to look more closely at reproduction. Again no threshold could be established. And I should say these conclusions are the same that were reached by the U.S. EPA, the Environmental Protection Agency, in its review of the scientific and medical literature on TCDD last summer. So in two of the very important areas of the effects of dioxin, that is on the liver and on the reproductive system, we can't find a dose that doesn't have an effect.

Now, the other area, which is very important, and, of course, is a major area of concern about dioxin, has to do with cancer. And here we have to look at another part of those dose-response, dose-effect curves to get an understanding of what's going on. Once again we are looking at dose and we are looking at effect. Only this time, of course, the effect is tumors, as we are talking about, tumors, that's the number of animals that are going to get a tumor.

Q Now let me interrupt for a minute, Doctor. At least in my vocabulary I don't necessarily equate tumor with cancer. Because I've got moles on my back, which I know are tumors and hopefully they are not cancer. At least they are not malignant. All right? Now, when you use the word tumor and cancer, is that synonymous?

A In the animals what has been studied has been malignant tumors.

Q Malignant tumors?

A Malignant tumors.

Q All right.

A There is a concern, of course, benign tumors may be a precursor or a warning of malignant tumors in animals and in people. And, of course, in cancer we also include leukemia.

Q In the word cancer?

A Yes. Leukemia is a cancer of the blood forming organs. It is a cancer.

Q So when you are talking now about these tumors, you mean malignant tumors?

A These are tissue tumors. That's what has been measured in the animals.

Q Malignant.

A Malignant tumors in the animals.

Q All right. Please go on.

A Now, the other parameter or the other knowledge that scientists have to bring to bear when they are looking at dose-effect relationships and they are talking about whether or not there is a no effect level or a threshold is to have some understanding of how the compound has acted. Now, we

don't yet know how dioxin is really affecting reproduction in all the different ways that it affects reproduction. We are doing some work on certain aspects of it, other people are working on other aspects. But when it comes to cancer, we have in fundamental ideas from molecular biology about what causes cancer, what goes on inside the cells that leads to cancer. And those theories, which are not just hypotheses, they are based on real experiments and real understanding of what goes on inside a cell. But what we know about the molecular biology of cancer tells us that there is no threshold of anything that causes cancer. That all that it takes to cause a cancer is for one bit of DNA inside one cell to be broken or otherwise altered and for that cell then to start cloning. That duplication itself with this abnormal broken DNA keep on dividing, and that is a tumor.

Q Now Doctor, are you talking about-- When you say cell, do you mean molecule?

A It may take just one molecule off a carcinogen to cause this, because you can have just an alteration in one part of DNA.

Q And that can start a process of growth of malignant tumors in the human and animal body?

A That's right.

Q One molecule?

A That is the molecular biology of cancer. That's why molecular biologists draw these as straight lines without a threshold and why the President's Office of Science and Technology Policy, which is preparing a government document on cancer and chemicals, states also that for chemicals that cause cancer there is no threshold, there is no level that does not have an effect, that does not in this case increase the risk of cancer in people who are exposed. And there is a great deal of experimental evidence done on cells exposed to chemicals, human cells as well, to show this concept of a one-molecule attack on one part of DNA being sufficient to cause this to happen.

Now, in addition, of course, as we mentioned yesterday, one of the frightening things about dioxin as a carcinogen is that if they do this, that is prime or initiate the cell, getting it ready to be malignant, we know it also does this, promote that cell that's already been altered, and it promotes it better or worse than anything we have ever encountered.

Q Doctor, back to the other chart for a moment. And hopefully you don't take this as being a male chauvinist, but you have talked about the female reproductive facility being affected and there is no effect level. What about the male reproductive system. How does dioxin affect it?

A Dioxin does affect the male reproductive system.

It is selectively taken out and stored in the male gonad in the testes and in the male gonad it does cause damage to cells in that gland, the cells that make sperm, and it also affects hormone metabolism, metabolism of testosterone and androgen. The hormone that man are dependant on to make sperm and other things as well, are also damaged by the presence of dioxin. Now, the studies that have been done on male reproduction and TCDD have been relatively few, and I don't think anybody would claim that we have enough information to say that there is a threshold or there isn't. We have really been working in relatively high doses.

Q You haven't worked enough on the males to know whether or not there is a no effect level or not?

A Right. But from what we know about the females I think the strong assumption would be that there is possibly no threshold for male reproductive effects either.

Q All right. Anything else about the no observed effect level?

A No.

Q These no L or no observed effect levels, are they published in recognized medical and scientific journals, this work?

A You mean this work on dioxin?

Q Yes. That you have discussed regarding dioxin?

A Yes.

Q And for how long has it been known that there is, as far as dose, amount of dose is concerned relating to these that you have just discussed and these two, better make them exhibits, two pieces of paper here, how long has it been known that there are no effect levels, as you have described?

A For the effects of TCDD to cause cancer, ever since it was first demonstrated primarily through the work of Dr. Kaseba (sp) of Dow Chemical in the middle 1970's, it has been known that as a chemical carcinogen dioxin didn't have a threshold or a no observed effect level. With respect to these other effects, that's relatively more recent, from about 1978 through the present time.

Q All right. And does the EPA and NIH, NIOSH, make regular pronouncements or, not regular, but do they announce from time to time where there is levels with relation to different drugs and chemicals that there are no effect levels or there are levels at which something can be safe?

A Yes. In the process of making regulations on chemical safety the EPA always evaluates that possibility.

Q Now, has anyone found just in general as far as safety is concerned that dioxin is safe at any level? And I am not just talking about no affect now, but I am talking

about in general terms of safety has anyone said that at a particular level dioxin is safe?

MR. HEINEMAN: Your Honor, I would like to object to the form of that question as being so broad and indefinite it is surely calling for speculation even on the part of this witness.

THE COURT: Overruled. If it's in the literature I think she would be able to testify as to it.

MR. HEINEMAN: If it's in the literature.

THE COURT: Overruled.

A Well, I don't think anyone has and I would prefer to cite the comments of Dr. Vernon Houke (sp), who is the Director of the Center for Environmental Health of the Centers for Disease Control, which he said that he doesn't like to use the word safe next to the word dioxin.

Q Now Doctor, what is meant when one says biodegradability of a substance? What does that mean?

A That's the ability of a chemical to be reduced in toxicity by biological mechanisms.

Q And by biological mechanisms do you mean by that those mechanisms that occur naturally if a chemical is left alone? That is, not treated.

A It may.

Q And has there been work performed as to determine

whether or not dioxin will degrade in nature or in undisturbed form other than by being disturbed by nature, the forces of nature, if it was just left lay around? Has there been work done in that respect?

A Yes, there has.

Q And what does degradability mean? Does that, in fact, mean loss of toxicity or disappearance in the atmosphere or disappearance all together?

A No. It means specifically that the parent compound, in this case TCDD, can be changed into another molecule which is less toxic.

Q But still toxic?

A It may be. It does not, however, refer to a situation where dioxin might be attached to dust on top of a road and a wind comes along or a flood as in Times Beach and moves that soil some place else. That is not degradability.

Q That is just movement. It didn't kill the dioxin.

A Didn't change the dioxin. Now, as far as the people right by where it used to be may feel it has gone away, that somebody else has it in their front yard.

Q All right. Now, what does half-life mean, Dr. Silvergeld?

A Half-life means the amount of time it takes for a substance, for half of a substance, 50 percent of the substance

to disappear.

Q Why do you scientists talk in terms of half-life?

A Because it is very hard to know when a substance is all gone. It may be because we just can't measure it down to those low enough levels to be absolutely certain it's all gone, but we can measure when half of it is gone.

Q Now, tell us, please, whether or not dioxin is biodegradable.

A In terms of living organisms in the environment, basically bacteria and other organisms in the soil and air and water, these organisms do not degrade dioxin, TCDD, to any great extent at all. The only degradation of dioxin which may occur is primarily physical. That is, it is not living systems which attack dioxin. But it appears to be. If there is any degradation at all it is either through the attack of water or sunlight on dioxin.

Q And does sunlight attack and does sunlight destroy dioxin in natural surroundings?

A No. When TCDD is adsorbed, that is attached on to soil particles or other organic matter, it is not degraded by sunlight.

Q Now, let me add for a moment. There is the word absorb, a-b-s-o-r-b, and the word adsorb, a-d-s-o-r-b.

A That's right.

Q And you said adsorb.

A Adsorb.

Q What's the difference between adsorb and absorb, a-b-sorb?

A Absorbed with a-b means something has actually taken up into other material, dissolved or taken up. And adsorbed means that it is very tightly attached but it is still separate and distinct from that other material.

Q All right. And does sunlight have the ability to degrade or speed up the half--well, create half-lives, if that's a proper statement, when applied to pure TCDD in the laboratory for instance or on a slide put out in sunlight?

A Yes. If TCDD is dissolved in a solvent like benzene and exposed to sunlight or to UV light, which is the part of sunlight which does the degrading, then it will degrade. Primarily the chlorines will come off the ring and then the ring will break up at the oxygen molecules and then it will degrade, but, of course, that situation doesn't exist in the real world.

Q Well, what about in the real world when dioxin is adsorbed to soil particles. Will exposure of those soil particles to ordinary sunlight in this latitude and this as we are here, will that sunlight, ultraviolet light, degrade or make dioxin not toxic?

A Not at any measurable rate. In fact, the measurements that have been taken, for example in Saveso where they have been monitoring the soil contamination around the ICMESA Plant over the years since the explosion.

A Since '76?

Q Since 1976 there has been routine monitoring by the International Commission, and the latest reports of that commission, which have been published, indicated that they can't compute a half-life. That is, not enough has yet been degraded, haven't reached the point where 50 percent is gone. So you can't tell how long it's going to be to get there.

Q And when was that last report published?

A In December of 1983.

Q All right. And the explosion took place in Italy in 1976, so there has been at least seven years that have passed since that explosion. And some authorities, some official people, doctors and scientists, have been measuring the life of the dioxin as it is adsorbed to the soil and buildings and trees and I suppose everything else in and around Saveso. Is that what you are saying, Doctor?

A That's right.

Q And they have not yet determined-- You all right, Judge?

THE COURT: I'm okay. I think this chair just lost

a wheel. Go ahead. I'm sorry to interrupt.

Q (Mr. Carr) They have not yet-- Might be talking about your half-life.

Have not yet determined that the dioxin at Saveso has reached a half-life as yet, even after seven years?

A That's right. They have been unable to and they have published this and stated that they do not yet know the half-life of TCDD in the real world environment, and they estimate that it has to be at least ten years, based on the shape of the curve they have got so far.

Q All right. But do they know for that matter that that dioxin even at the end of ten years will have reached half of its life?

A No, they don't know for sure. That is a prediction.

Q And does this half-life mean that--just hypothesizing that it will reach its half-life at three more years from now, that at that time that dioxin yet remaining will have then a life of ten more years?

A It means this. Let me draw you a half-life curve. It doesn't mean that it is all gone in ten years, of course. And the seriousness of it of course depends on how much you start out with. But half-life calculation is this: Here is time, which I guess we ought to put--let's say it is ten years. Let's say they turn out to be right, it is ten years

Here is twenty years. Here is thirty years. Here is forty years. And you start out with a certain amount of TCDD. That means in ten years you are down to half as much as you had. In twenty years you are half again, you are at 25 percent of what you originally had, because that's half of 50 percent. At thirty years you are down to one-half of 25 percent, or I think that's 12.5 percent. In forty years you are down to half of that again, which is 6.25 percent. So you can see you are not--while it is going down you still certainly have very measurable amounts going on as long as forty years.

Q Now, if we started out say with 45 parts per billion TCDD at the first year. In ten years from now that would be 22 and a half parts per billion?

A If this were right this would be down to 22.5.

Q And twenty years from now it would be down to 11 parts per billion?

A Yes.

Q And thirty years from now it would be down to 5 parts per billion?

A Uh huh.

Q Five and a half parts per billion?

A Uh huh.

Q And forty years from now it would be to about 3, 2.8 parts per billion?

A Right.

Q And fifty years from now it would be down to 1.4 parts per billion?

A That's right.

Q And sixty years from now it would be down to .7 parts per billion?

A That's right.

Q Sixty years from now?

A That's right.

Q Just then we reach the under 1 part per billion level, would be sixty years from now?

A That's right.

MR. CARR: Your Honor, I think this would be a convenient point for a recess, if it's all right with the Court. You can fix your chair, or have Ralph fix your chair.

THE COURT: Ladies and gentlemen, we will take a break at this time from the testimony. I will admonish you now and these hold for the rest of the day, that you are not to discuss this matter among yourselves or with anyone outside the jury panel and you are not to form any opinions about the matters on trial.

Thank you.

The Court is in recess.

* * * * *

THE COURT: Mr. Carr?

Q (Mr. Carr) Dr. Silvergeld, we have talked about biodegradability and the half-life of dioxin. What does the word bioaccumulation mean?

A It means the ability of a substance to be stored in living organisms at a level and amount greater than that which is outside the organism.

Q The bio always means life?

A That's right.

Q So when we have biodegradability, we mean the degradability in life and living things. And when we say bioaccumulation, the accumulation of things in living organisms?

A That's right.

Q Has there been research work and scientific conclusions reached relative to bioaccumulation, that is, accumulation of dioxin in living beings?

A Yes. 2,3,7,8-TCDD is accumulated in living organisms, including humans.

Q Now, where is it accumulated or how is it accumulated?

A It is mostly accumulated in fat, because as I mentioned earlier, it has a very high preference for fat that's known in scientific terms as being lipophilic.

Q Let me stop there for a moment. You say it has a high preference for fat. That sounds as if you are saying

it has some kind of an intelligence. It wants something and it's going to get it. And I am sure you don't mean that. I don't think you mean that.

A No.

Q What do you mean when you say that it prefers fat?

A Because of its chemical structure it is much more easily dissolved in fat.

Q That was that drawing you made the other day, then, of the levels of water and things of that sort?

A That's right.

Q All right. Now I'm with you.

A That's right. And so when dioxin enters the body and is transported throughout cells it is accumulated in fat. That is, it is stored in fat. And once it is stored in fat, and as I mentioned, fat is not only fat cells underneath our skin, but is also the membranes of all cells which contain fat and very much it is the wrapping around our nerves, which is very fat rich. That's the areas where dioxin goes. And once it goes there it's not metabolized very quickly at all, because those are cell systems that don't have much metabolism of dioxin or other types of chemicals that are similar to dioxin.

Q That fat around our nerves and around the cells, that's a normal, good kind of fat I take it?

A That's right.

Q Supposed to be there?

A That's right.

Q All right. And dioxin is stored in all of those fat cells wherever they might be in the body?

A There is also a distribution of dioxin among different organs in the body. That is, it doesn't go to all the organs of the body on a kind of equal basis. But it does appear to go to certain ones more than others. But it's in those organs that dioxin then moves into the fat and is stored for a long period of time, and that's why over a long period of time, even if the person or the animal is exposed to low doses, those will build up in the body, and that's what's known as bioaccumulation.

Now, the EPA, the Environmental Protection Agency uses bioaccumulation, that concept, as one of the ways in which they develop standards to protect our health against chemicals like dioxin, and they use it in the following way: They assume that if there were dioxin in water, there is two ways--and they have just written a water quality on dioxin, which I was one of the reviewers of, and this is what the EPA said: If there is dioxin in water there is two major ways you are going to get exposed. You could drink the water or you could eat the fish which had been in that water. Now, when you

drink the water, we will estimate this is how much water you are going to drink, and this is the exposure you get. In addition, however, you might eat those fish, and the fish are going to bioaccumulate the dioxin out of the water, and the rate which they do that is a measure of how much more dioxin, TCDD, is in the fish than is in the water. And that number indicates just how tightly stored dioxin is in animal and human tissue as compared to the rest of the environment. For TCDD that number ranges between 10,000 to 40,000. That means that for a fish swimming in water, that fish will have 10,000 times as much TCDD in its fat tissue as there is in the water around. And that indicates that this is a very highly bioaccumulated substance. The same thing will go on with people.

Q If there is 1 part per trillion, let's say in the water just for instance, when that fish living in that water, using that water, its body, its tissue will accumulate that dioxin so that instead of being 1 part per trillion it would be 10,000 parts per trillion, which would--well, 10 parts per billion then, would it not?

A That's right.

Q Now, has that been demonstrated to occur in tissues, living animals other than or in addition to fish?

A Yes, it has.

Q And--

A And indeed its been demonstrated for human beings.

Q How so?

A There have been recent studies undertaken by the U. S. Air Force in connection with the University of Nebraska and the Environmental Protection Agency to come to an understanding of how much dioxin there might be in our own bodies. They have looked at people who served in Vietnam. They have looked at a range of people. And they have taken actual samples of fat from people and measured dioxin. At the same time they have measured the amount of dioxin in those people's blood. Now, that's a kind of similar situation as the fish swimming in the water, if you think of it, because your blood is the waterlike or aqueous substance flowing through your body and the tissue is the fat part or the fish, if you will. And the ratio between what's in the blood and what's in our fat is very similar to 10,000 times difference.

Q Dr. Silvergeld, translated to terms more pertinent to this case, if one were exposed on an every day basis for a period of years to small amounts of TCDD, say 1 part per trillion or 65 parts per trillion or some other measurable--some other amount. Would that person by living in that community and associated with those low amounts, would that dioxin be accumulated over a period of time in that person's

body?

A It would.

Q And at the rate of 10,000 times the amount, or 10,000 to 40,000 times the amount to which he is exposed on a daily basis?

A If the person were exposed long enough to a continuing source of TCDD, eventually the difference could be as great as 10,000 to 40,000 times.

Q Now, that 10,000 times the one trillionth part per billion of TCDD, over what period of time would it take for that to bioaccumulate in the human tissue, so to speak, so that it would reach 10 parts per billion or 1 part per billion? Has there been studies done on that level?

A No, there really haven't been. But certainly that possibility is why the Environmental Protection Agency, the Centers for Disease Control, New York State, the Canadian Government, the Italian Government, and many other authorities have set the standards for dioxin exposure so very low. That's exactly what they had in mind.

Q The people at Saveso, Italy, how long were they actually exposed to the TCDD contaminant before they were evacuated from Saveso?

A I think it was between ten and twenty days.

Q And the soldiers in Vietnam that have been exposed

to agent orange, for what length of time have those soldiers from Vietnam been exposed to agent orange?

A I think the group that is thought to have been exposed for the longest, this is according to the Department of Defense records, is between two and three years.

Q And our incident in Sturgeon took place in 1979. That's now five years ago.

A That's right.

Q Is it fair to say, then, that so far as you know the people at Sturgeon, if they are exposed to TCDD, have been exposed to these levels, and if there is TCDD there, have been exposed to TCDD for a longer period of time than the soldiers in Vietnam and the people in Saveso before they were evacuated?

A Yes, they have.

Q Doctor, what about the ability of the human body to degrade, to destroy, to dispose of TCDD so that it will not accumulate in the body? Doesn't it have that ability?

A Yes, it does.

Q Then why doesn't it dispose of, why does it permit the accumulation of this substance? Don't we have organs like the liver and the kidney and things of that sort that's designed to get rid of foreign substances or unwanted substances?

A We do. And there are several reasons why this

doesn't work so well for TCDD. One is that TCDD is partitioned away from those enzymes. That is, it is taken up by the fat, and those enzymes aren't that active in fat cells as they are in other cells. So it's kept away from the metabolic factory that might take care of it. The other is, as I mentioned earlier, yesterday when we were talking about the metabolism of TCDD and its molecular effects, is that TCDD effects its own metabolism. So it has an interference with the very pathway that should be taking care of it. And the third reason is that TCDD damages the liver. It actually kills liver cells. And thereby impairs the ability of the liver to handle TCDD itself.

Q When these porphyria abnormalities are found, is that an indication, at least in the laboratory, indication that the liver has indeed been damaged?

A It's an indication of a specific type of liver damage, yes.

Q Now Doctor, the TCDD accumulation, if it accumulates in fat and stays there, how can that hurt the human if it just is in that fat, accumulated in that fat?

A Well, it can be harmful in several ways. First off, if that fat is the fat membrane around a cell, TCDD in that membrane can be causing those changes in that membrane function we talked about yesterday which lead to immunosuppression,

that is failure of the immune system, and also promotion of cancer. So just being in the fat is not a safe place to be. The other possibility is that if TCDD is stored in those fat cells that wrap around nerves, that provide the insulation for our nerves in our brain and the peripheral nervous system, it will slowly degrade that wrapping, and that is the demyelination neuropathy that people talk about when they describe the clinical signs of TCDD poisoning. And the final thing is that TCDD, like other substances similar to it, like DDT for example, or lindane or dieldrin, can be mobilized out of the fat. That is, a variety of physiological events, like pregnancy, like weight loss, can bring the TCDD back out of the fat and back into circulation where it can cause harm. One very important way and very dangerous way in which this happens, and this has now been measured, is that when a woman is nursing a baby, TCDD will be mobilized out of fat stores into the milk preferentially, and then excreted in the mother's breast milk in the milk fat which the baby then is exposed to. And you can measure measurable amounts of dioxin in breast milk fat in women.

Q Doctor, this bioaccumulation in our cells, doesn't that TCDD that is accumulating there, doesn't it have a half-life? You discussed the half-life in nature and soil and the buildings, doesn't it have a half-life?

A The closest information we have to answering that question--of course, we don't have half-life information on people. To do a half-life study you have to administer a certain dose that you know you have measured to a subject and then you have to basically take that subject and extract all the dioxin out to see how much is left. With animals, of course, that can be done and it has been done. And what we know is that one small dose of TCDD given to a rat or a mouse, the half-life, the amount of time it takes for half of that dose to go away, is approximately thirty days. Now, that's a relatively long time for a drug or a chemical to stay in the body, and that's just one dose, and a small dose.

Q Well then, Doctor, if it has, assuming for a moment that these animal studies can be extrapolated and are useful in determining what happens in human beings, as you have indicated, can we not conclude then that the bioaccumulative effects of dioxin isn't really so bad, because after all it only has a half-life of thirty days?

A Well, let me draw you one little picture to show what happens when you deal with something to which you are continually exposed and it has a relatively long half-life. Thirty days is not short for a compound. Most of the drugs we deal with have half-lives of hours or minutes, to give you a comparison.

What's going on, if we could do this study in people, and we could do it, of course, in animals, this is the kind of thing that's going on. Here is time again, just like our other half-life curve. This is for biological half-life. Before we were looking at environmental half-life. This is also known as toxicokenetics, which is just the dynamics of what's happening to a toxic substance over time. And so this would be the amount of TCDD measured, let's say in the whole body, if we could do it. The exposure starts here. So at Sturgeon that would be when the accident occurred. In Saveso when the explosion occurred. It's a rapid uptake of TCDD into the body. It starts to come down. It comes down at a rate so that by thirty days half of it would be gone. But exposure is continuing, so you build on to that, you build on to it. I'm doing this curve wrong. But actually what you wind up getting is this kind of line, and that is the bio-accumulation. Let me bring this down to here so I can show it to you. So that as it is falling there is more coming into the body. It doesn't get a chance to completely disappear. When we drew that environment half-life curve we started out with 45 parts per billion and that was it. There was no more coming into the environment, so it started to slowly go away. But if a person or animal is continued to be exposed, as it is going away more is coming into the system. If you smooth this

curve out this is what you get. And this would be, this kind of line would indicate bioaccumulation.

Q In the first thirty days half of the amount of TCDD that was absorbed on the first day has had its life in the tissue?

A Right.

Q So at the end of thirty days, however, we still have half of that life left?

A That's right. It would look like this. Then you take on a second dose, which is the same as the first. Of course, this is occurring not just every thirty days, but let's just say you got exposed every thirty days, you come up here.

Q You have a base of a half-life to build on, is that what you are saying?

A You have still got half the stuff in your body.

Q Somewhere on this point is a base then, because the new is added to the old, you have a new base to build upon?

A Then you take on another dose which is the same that you got before, because the dioxin hasn't gone away, you haven't moved away, or whatever. You go up again and then it starts to decline, and then in another thirty days it's down to a half-life. But this is more than it was before. Then

you get another dose. It goes like this. It's the same dose. These doses are all equal. In thirty days you come down. This is now ninety days from the beginning of this episode. But you are moving up a line, which indicates an accumulation of this substance.

Q And so Doctor, if you had an acute exposure, that is a one-time substantial exposure to dioxin, it would accumulate in your body, but over a period of time the half-life effect would take place and you would have gradually lesser amounts. Even though you may have started out with a very large dose, over a period of time the half-life would diminish the amount that's in your body?

A That's right.

Q But a chronic, every day, long-time exposure to low doses in fact creates the opposite effect, it adds to the stored dioxin in your body?

A That is what is known as bioaccumulation.

Q All right.

A And that's how it happens, even with something which the body can eventually take care of.

Q Now Doctor, directing your attention for a moment to vehicles by which dioxin might get in to human bodies. As far as dioxin itself is concerned, you have mentioned that it adsorbs or adheres to soil particles, is that correct?

A That's right.

Q How does that soil particle to which dioxin is attached, how does that get into the human system so as to allow it to get into the fat, so as to allow it to get into the liver, and so forth, on the soil particle?

A Well, soil particles are taken up by the even gentle movements of air or people walking across a dusty area or cars driving by. That whole process is known as entrainment by which particles are taken up into the air, and then when we breathe air we then inhale along with the air a measurable amount of soil particles.

Q Even though we can't see it?

A We may not see it, we may not even be aware of it. But even in a room like this, the National Institute of Occupational Safety and Health has measured measurable amounts of soil particles. Obviously, when you are outside it's even higher. If it's an area where it is dry and dusty on farms and dirt roads and vehicles moving over those dirt roads, or kids playing in a dirt schoolyard, whatever, there will be even more dust kicked up into the air. It's only when it is very dusty that we notice it's dusty, and we say oh, my goodness, I'm breathing a lot of dust, and some people might be irritated.

Now, depending on the size of those soil particles, that inhaled dust or surface soil will either go deep into the lung

and be taken up by the lung, or the chemicals attached to the soil, absorbed off the soil, adsorbed off the soil particles into the blood stream. Or if the particles are slightly larger and the magic dividing number seems to be 10 microns in diameter, that is, if they are smaller than 10 microns, these soil particles will penetrate deep into the lung and be taken across the lung barriers into the blood. If they are slightly larger than 10 microns in size--these are very small, of course--then they move back up and are swallowed. And you probably have had the sensation of when you are in a dusty area outside of feeling the need to swallow, and what you are doing is swallowing the dust particles that you have inhaled. So then you are directly ingesting the soil. So through soil in the air you have the possibility of an inhalation exposure and an ingestion exposure.

Q All right. The-- I interrupted you, Doctor. Go ahead.

A Another way you can be exposed, of course, is to get the soil particle on your hands, on your food, surface water, or anything that's out that you then put in your mouth. And everybody engages in a fair amount of hand-to-mouth activity. Going like this.

Q Right now my hands up against my mouth.

A That's right. That's hand-to-mouth activity. And that can transport a measurable amount of soil or dust into the

body by ingestion.

The third way in which dirt, contaminated dirt, could lead to human exposure is by contact. And that is chemicals can actually, if the skin becomes covered with dirt, some chemicals may detach themselves from the soil and be taken up through the skin barrier.

Q Well, what about TCDD? You said it adheres, adsorbs to the soil. Does the dust, if there are some dust molecules or particles that have TCDD, adhere or adsorb to it, if it lands on the skin is there any likelihood that that dust, that TCDD from that dust could be absorbed?

A Yes. There have been several studies on the subject, because people are very concerned about circumstances where TCDD has contaminated soil, in Missouri and elsewhere.

Q Doctor, doesn't that contradict the hypotheses that this TCDD binds tightly to the soil and stays on that soil molecule?

A Well, the surface of your skin is an active biological area, and so--

Q What do you mean?

A So there are processes going on. There have been studies done at New York State Department of Mental Health and at the National Institute of Environmental Health Sciences, part of the NIH, a federal agency, which have looked at the ability

of animals, obviously, to take up dioxin, TCDD, when it's bound to soil or to soot, from the Binghamton fire, when this complex of soil and dioxin, soot and dioxin, is either rubbed on the skin or fed to the animal. And what was found, much to some people's surprise, was that that dioxin, that soil-bound dioxin, is very bioavailable. And Dr. McConnell at NIEHS estimates, in fact, that if you feed an animal TCDD bound to soil, and what he did was take soil from Times Beach, so he didn't make something up in the laboratory, he took a real world sample. When he fed that to animals, he estimated that somewhere between 30 and 60 percent of dioxin bound to the soil moved across the gut into the animal.

Q What about the dust particle on the skin, though, Doctor?

A The New York State scientists rubbed some soot from the fire, which contained dioxins and furans, on to the skin of animals and also found a measurable uptake. I don't recall how much it is at the present time, but they have published these findings.

Q Is there some biological processes going on in the pores of my skin that effects, that can cause the TCDD to get off the soil or off the soot and into my pores?

A I don't know as anyone has looked to the mechanisms by which this could happen.

Q But they know that it does happen?

A It does happen.

Q All right. Now Doctor, what about the effect of sunlight on these dust--because when it turns into dust its got to be on a summery, sunshiny day. It can't be wet for it to be dusty. When it turns into dust and the sunlight hits it, doesn't that sunlight destroy that dioxin?

A Well, the environmental measurements that have been done would indicate that it does not.

Q The environmental measurements at Saveso?

A Mainly at Saveso and also in Missouri.

Q What do you mean by that, Doctor? Where in Missouri have they found that sunlight won't kill dioxin?

A Well, the Environmental Protection Agency and the Centers for Disease Control tried a great number of emergency strategies to deal with the problem of the many dioxin sites that were identified in Missouri over the last couple of years. Including increasing the exposure of soil to sunlight, and they were unable to have a measurable effect on the concentrations or degree of contamination of TCDD. Now, studies have been run by the U. S. Air Force in which they reported that sunlight exposure of surface dust contaminated with dioxin did degrade dioxin. But to my knowledge no one else has been able to reproduce those findings.

Q The dioxin that's in the soil and in the dust at these various places at Missouri, are the horse arenas, the horse arene matter included in those places where they have determined whether or not sunlight will destroy the dioxin?

A I'm not sure if they used the horse arenas or Minker-Stout residential sites which had dirt which was taken from the horse arenas. I'm not sure which of those sites were used.

Q But the studies have been done with actual, in life conditions on dirt as to whether or not the sunlight getting to that dirt that's in the community will destroy it?

A That's right. And also at Saveso there were attempts to determine whether the surface dust would be reduced in contamination over time in the most contaminated zones at Saveso.

Q Now Doctor, I think you have explained how dirt particles to which TCDD has been adsorbed or adhered can come into the human system. Does dioxin have a degree of volatility as far as can it turn into a gas or vapor and come into the atmosphere that way independently of being attached to dust particles?

A Yes, it can.

Q Could you explain that, please?

A Well, my answer is based on my experience on the

Governor's Blue Ribbon Panel for the State of New York related to the Binghamton State office building. What we have had to deal with there, as you may know, is a building in which a transformer was involved in very serious fire. As a result of that fire the contents of the transformer burned. And the contents included polychlorinated biphenols and chlorobenzenes. Chlorobenzenes are molecules that are very similar to chlorinated phenols. When these contents of the transformer burned they produced, as many people knew they would, dioxins and dibenzo-furans, which are chemicals very similar to dioxins, including 2,3,7,8-TCDD. The building was shut down almost immediately after the fire and a long process of decontamination and clean up has been undertaken by the State of New York. This advisory committee, which I have been on, has been overseeing the clean up, looking at the data that has come in, making recommendations to the state as to whether or not the building can be opened, whether people can go back in, and what should be done. To date we have been in agreement that the building cannot be reopened and people cannot go into it. One of the things that has happened over the three years since this fire has been the realization based on real data, not theoretical calculations, that dioxins and furans are actually being volatilized into the air inside that building. That is, they are moving from a phase where they were, like soil,

adsorbed tightly on to ceiling tiles, floor tiles, hidden recesses in the building that weren't clean, but this pool of dioxin, if you will, apparently continues to provide a source of volatile toxic material which comes out into the air of the rooms. And that's one of the reasons why that building can't be reopened.

Q Doctor, was that more or less predicted by the example that you mentioned that came from Germany when they had an explosion or an accident in one of those plants where they took the cages that had been in the plant that they had the rabbits in and they took those cages out of the plant, put the rabbits in those cages, and those rabbits died in the cages? Would that be a predictor or an indicator that TCDD does volatilize in that fasion?

A I don't think anyone has ever thought of it that way, but I think that's absolutely right.

Q Maybe I have contributed something to science.

A I think that's very consistent.

Q Does it have the same volatility for instance on something like phenols would?

A No. Based on the physical chemical parameters of dioxin it would have a much lower volatility. But I hedge a little bit on that, because I think what we are observing in the Binghamton office building, and I stress this building has

not been heated, because it is not being used. The only people that are going in there are in moon suits trying to clean it up. I think that the movement of dioxin into the air, into the vapor phase, requires a lot more investigation, because it seems to be much more frequent in occurrence at lower tempuratures than we had predicted.

Q Now, what's the significance of the lower tempuratures as far as volatilization is concerned? Are there tempuratures at which chemicals such as TCDD can be more volatile than at other tempuratures?

A Volatility, that is the ability to become a vapor phase, is dependent on tempurature and atmospheric tempurature. So that if you raise one or the other you will increase the volatility of any material.

Q And Doctor, is what you are saying that the Binghamton experience, because there was no heat, is that in Northern New York? Where is that?

A That's in upstate New York.

Q It gets cold up there?

A It does.

Q And there was no heat in the building during the winter months?

A No.

Q And did I understand you then to say there was some

volatilization of TCDD even in the cold winter months?

A I'm not sure all the months that have been measured, but there certainly was measurable volatilization of dioxins as late into the year as November, which in upstate New York is pretty cold.

Q Now, TCDD in the soil. Say it's covered with a layer of rock or overgrowth. Does it have the capacity to volatilize if it has not got an impermeable cover over it?

A Absolutely. The only thing that will stop a vapor is a truly impermeable sealing layer. That is, a layer that seals. That's one of the methods that's being proposed to use in Binghamton, because it is a very similar situation there. You have a room say this size in this office building. All the ceiling tiles have been removed and replaced. All the light fixtures have been removed and replaced. The floors have been washed, they have even been replaced. The walls have been replaced. New walls, new ceiling, new floor in place, and still vapors are coming through.

Q In this completely replaced room?

A That's right.

Q Where are the vapors coming from, Doctor?

A The deep recesses, electrical conduits and other parts of the building where those particles of soot with the dioxins and furans were attached, were driven by the force of

the fire.

Q And even though it is sealed off by ordinary building material, walls and that sort, it still is vaporizing and still coming into the room?

A That's right. It has not sealed off from the point of view of a chemist.

Q And that kind of sealing off, is that described by, when you say they went into these rooms with moon suits? What is a moon suit?

A A moon suit is I guess a common name for the kind of outfit that the Environmental Protection Agency has recommended as the standard gear for people to wear when they are going into an area of dangerous chemical contamination. It is usually at least two suits. One is a disposable paper suit which is worn over the clothing. Then on top of that is a plastic-treated suit which is resistant to ripping and tearing. It is all tied off very tightly at the ankles and wrists. It has a hood covering over the face, respirator. Can even be an enclosed air supply, like a diver's apparatus attached or just a series of filters, depending on what's encountered. A couple of layers of gloves. Chemical resistant rubber on the outer gloves. Same kinds of things on the feet.

Q Now Doctor, as far as the volatility of dioxin is concerned, is it correct then that what you have said is there

is more volatility, more apt to be vaporized in warm or hot weather than in cold weather?

A Yes.

Q Doctor, what about the solubility of dioxin? The ability of water to dissolve and flush it away. Has there been work done in that respect?

A Dioxin is relatively insoluble in water. That is, it does not dissolve in water. That's part of its property of being lipophilic, as we talked about before in biological terms.

Q If dioxin molecules were attached to organic material such as you find in soil, or attached or adhered to the soil itself, would washing that soil with water dissolve the dioxin from that soil and move the dioxin out?

A No. I think we had an example of nature trying to do that in Times Beach, and all that happened was the soil particles with the dioxin attached were moved around.

Q What about the soil particles that didn't move? The large body of dirt that's not moved by water, does that dirt, that solid attached to the ground or whatever it is that doesn't move, does that dirt get the dioxin washed out of it?

A No, because dioxin will not dissolve in water.

Q And is what you are saying, you could wash, if dioxin is in a box of soil, for instance, and you washed that box of soil day and night for a year, that it would not dissolve the

dioxin that's in that soil?

A Not to any appreciable amount, no.

Q If the soil were capable of being eroded or soil particles moved away from that box, suppose you had holes in the bottom of the box and you flushed the water and you dissolved some soil from that major body of soil, would those soil particles that you are flushing out of that box, would they have dioxin adhered to them?

A Yes, they would. That's very similar to the Times Beach flood.

Q And would that dioxin then move with that soil particle so far as the water allowed it to move?

A So far as the water moved the soil the dioxin would move with the soil.

Q And if the dioxin, if this soil reached a pond, a pool, would the soil have a tendency to drop to the bottom of that pond or pool?

A Given the right characteristics, yes, it would settle out.

MR. CARR: Your Honor, this is I think a convenient place and it's just about noon and Dr. Silvergeld has to catch a plane in a very short time.

THE COURT: Fine. Okay. Thank you.

We will break in the testimony for today. As I explained,

this afternoon I have a criminal matter that I have to try. So we will not be holding court this afternoon as far as this cause is concerned. I would appreciate it if you would be back in the courtroom at 9:30 Monday morning. At which time we will resume testimony. I admonish you that you are not to discuss this matter among yourselves, with anyone outside the jury panel, or reach any opinions or conclusions about the case. And since this is an overnight break for a weekend, I would further admonish you that you are to avoid reading or listening or seeing anything about the case or the general subject matter of this case in either the print or electronic media.

Thank you for your attention and cooperation.

The Court is adjourned. Have a nice weekend.

(COURT ADJOURNED)

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STATE OF ILLINOIS)
)
COUNTY OF ST. CLAIR)

I, KAREN D. HOPKINS, C.S.R., Official Court Reporter in and for the Twentieth Judicial Circuit, do hereby certify that the foregoing transcript is a true and accurate record of the proceedings had on the 13th day of April, 1984 in the foregoing entitled cause before Honorable Richard P. Goldenhersh.

Dated this 16th day of April, 1984.

KAREN D. HOPKINS, C.S.R.

STATE OF ILLINOIS)
)
COUNTY OF ST. CLAIR)

I, HONORABLE RICHARD P. GOLDENHERSH, Circuit Judge in and for the Twentieth Judicial Circuit, do hereby certify that the foregoing transcript is a true and accurate record of the proceedings had on the 13th day of April, 1984 in the foregoing entitled cause had before me.

Dated this 16th day of April, 1984.

HONORABLE RICHARD P. GOLDENHERSH