Alison0:06

Alright, so the second part of the of the draft is for endocrine disruptors, and this is tougher. It's much more difficult because the criteria are less clear. And there's also some overlap with some of the existing hazard classification, particularly stopped, I think is where the where the overlap lies.

So what we have is we have endocrine disruptors for human health, and then we have a second hazard classification which is endocrine disrupting substances in the environment and it breaks down similarly to CMRs in that there's a category one which is for known or presumed substances and then category 2, which is for suspected substances.

Janet Greenwood0:59

And again, that's very like carcinogens, for example, or reprotoxicity. Yeah, we definitely know this (*category 1*). And we've got a strong suspicion (*category 2*). Yeah.

Alison1:04

Exactly, yeah. And it's designed whereby you are looking at studies on animals then you must assume that that is relevant for human effects, unless you can conclusively show that that is not the case.

So you must have evidence that it is conclusively not the case in humans,
Otherwise, you must apply the data.

Janet Greenwood1:40

And that's the precautionary principle coming in, isn't it?

Alison1:43

Exactly, yes.

I think the the thing that …. I wanna say the thing that bothers me.

Janet Greenwood1:51

No, you're perfectly entitled to say it bothers you.

Alison1:56

So essentially what you're looking to prove is that it meets all three of the following criteria, and the first is that there's endocrine activity. Fine.

There's an adverse effect .Fine,

But the third one is that there is a (and the term used is) “biologically plausible link” between that endocrine activity and the adverse effect.

And it's the “biologically plausible link” that bothers me.

Because the definition that's given for biologically plausible link is that it is the correlation between one or a series of biological processes, leading to an adverse effect and an endocrine activity.

So it uses the word correlation now personally “Correlation isn't causation”,

Yeah biologically plausible

Janet Greenwood2:54

Correlation is not causation. How how many times, how many? How many times has that been drummed into us at school? At university?

Correlation is not causation, and here we have the regulator saying correlation is good enough.

Alison3:13

Yeah. So they're saying, you know, does the evidence line up? Does it sound about right that it caused it? Roughly ish,

Which I really don't like.

Janet Greenwood3:23
Yeah,

Can I also can I also give you a memory of mine going all the way back to 2003 now, I went up to the British Society of Soil Science “do” because we we were presenting a poster there. Well, I say we it was just me at the time.

And the chap who did it, I can't remember his name. He was a professor from the University of Michigan who had worked with 3M when they discovered the PFOS in polar bears (*blood*). And really interesting. He took it to the guy at 3M and he said we are not in the business of killing the world and they pulled it there and then pretty much they treated it really, really seriously. So 3M were completely responsible in that respect.

But he also was working on endocrine disruptors.

And he said, (very much as we do with toxicity and Paracelsus, the dose makes the poison), anything in sufficient quantity can be an endocrine disruptor.

It is one of these catchall phrases. It means what it says, it says what it means.

If you're British and you're familiar with Humpty Dumpty about the definition of words from Alice in Wonderland, it means what I mean it to, no more and no less.

And so in the definition of endocrine disruptors, we've got that twice -

- The term endocrine disruptor in the first place
- and then "Correlation".

Now, I want to ask you a question now. Like before we go into the nitty gritty of how this works, which is.

Do you think that the reason why the EC and ECHA are rushing this out is because they know they're kind of on shaky grounds technically?

Are they just trying to steamroller industry and everybody? Or do they genuinely believe it's just a technical issue which is their the reason why they've they're claiming that they're allowed to do this because it's just Annex updates, therefore it's technical?

Alison5:38

It's a little bit unusual in that they have published a little bit of the justification in this consultation.

So prior, at the very beginning of this Commission Reg, they published a few chapters that says, here's why we're doing this.

And this is very unusual. They wouldn't normally do this in a draft Commission reg., they would normally just say, here's the regulation. So to publish some of.

Janet Greenwood6:03

(*interrupting*) Because it's been to CARACAL and everybody's agreed it before it comes through, yeah.

Alison6:07

Exactly. You wouldn't normally say "Here's the process we went through and here's why we think it's justified in the reg". That's very odd for them to do this, which suggests they know that they're gonna get pushback.

And in the latest CARACAL, there is a 20 page justification document for why they're doing this and why they're doing it in this via this mechanism. So via an ATP rather than via full legislative act. And the same bullet points are given..

You know that "they need to do this under the chemical strategy for sustainability", that they're "doing it because it protects consumers, vulnerable group and work vulnerable groups and

workers" and then "it's part of their target of zero chemical pollution in the environment," which we all know that that phrase is meaningless.

Janet Greenwood6:50

Let's not go there. Let's not go there, because it's bad for everybody's blood pressure.

I mean, I must admit Darren Abrams from Steptoe (& Johnson) has a very interesting article which we can put a link in below, well a post on LinkedIn saying he thinks that really this should have gone through the normal processes. It's a big enough change to see CLP to have gone through the normal processes.

(Darren's post here: https://www.linkedin.com/posts/activity-6978276731325423616-96CK/)

And I just wonder if they're kind of steamrollering everybody they're trying to steamroller the GHS committee at the UN even.

Alison7:14

Yeah.

Janet Greenwood7:22

Because they're not that confident about it.

Alison7:25

They just make a point of calling out there. "Here's our justification. Here's the science. Here's you know, here's where we've done things like this previously. Yeah, here's. Here's where we've done things like this previously. And other legislation. You know, we think it's justified".

And to me, if something's justified, you don't have to stand there and go "here's all the reasons it's justified"

Janet Greenwood7:31

Sorry "the science". (sarcastic quotes gesture)

Exactly. Yeah. They're damning themselves by their actions to a certain extent.

But we have to leave that on one side for very, very clever people like Darren and the team at Steptoe, etcetera to deal with that. We're not involved in the politics of it.

We're just involved in the implementation, should all this go through.

So we've got this new endocrine disruptor hazard classes. Are they EUH statements in the same way as PBT PMT?

Alison8:13

Yes, and they're very unusual EUH statements.

They are EUH statements "in phrase", you know, they're prefixed with an "EUH", but again, they have signal words, they have precautionary statements attached to them and they are being inserted in Annex 1 rather than Annex 2. And they are being inserted into the hazard statement tables in Annex 3 rather than the EUH statement tables.

So to all intents and purposes treated like hazard statements rather than EUH statements, although they are technically prefixed with an EUH.

Janet Greenwood8:50
So that's exactly as we talked about in part one of this discussion, which is that they are effectively just almost waiting for a rubber stamp, which they hope to get from the GHS Committee and for these things to be adopted worldwide.

Alison9:03

Correct, yes.

Janet Greenwood9:06
Now, I know that we talked about this earlier. Do any of these endocrine disruptor EUH statements have pictograms.

Alison9:16
They do not. No pictograms, neither for the health nor the environmental.

Janet Greenwood9:21

Now that's a big change from what the original proposal was. I mean, this has been another non standard way in which this has happened.

It's been a bit like a magician pulling a rabbit out of the hat for endocrine disruptors because they put information out. I think it was a year ago, past January or something like that, saying this is what we're going to do.

And I remember they were going to have wheezy, man or gunshot residue or long term health hazard, whichever of the 50 or so different phrases we all use for long term health hazard.

They were going to have a pictogram's well, but they're not doing this in this case.

Alison10:01

They have not. I would have expected the health hazard pictogram. In all honesty, I would have expected the health hazard pictogram based on the rest of the language surrounding it and the criteria for classification. It seems like it would have lent itself to a health hazard.

Janet Greenwood10:18

And when you're saying that there is overlap with STOT, clearly if STOTs also apply, then you will get it.

But it sounds like there are certain criteria where they this is going to bring substances that are not and mixtures that are not otherwise classified into classification.

And therefore you would expect a pictogram, wouldn't you?

Alison10:40

I think that STOT is gonna be the main problem here, so I'm gonna pick out one phrase in particular here.

So it says “where the endocrine related adverse effects occur together with other toxic effects, endocrine related adverse effects shall be considered to be present where they are not conclusively demonstrated to be a solely nonspecific consequence of the other toxic effects”.

And that is slightly confusing language.

So I'm going to pick out an example here and what I'm going to pick out is the example of the toxicity of ethylene glycol or monoethylene glycol diethylene glycol and I'm gonna pick it out because it's a fairly well known toxicity fact.

And this is antifreeze for people who aren't familiar. So antifreeze is known to have a toxic effect, which is essentially that it causes you're in crystals to form in the kidneys.

Which causes long term toxicity and essentially people die from it. Which is why antifreeze has to be brightly colored with different dyes to stop accidental ingestion.

Janet Greenwood11:52

And if I can just add, it is much quick, more quickly, toxic to dogs. Do not let your dogs drink antifreeze. It's really, really bad for them.

Alison12:03

Now currently, this is dealt with with a with a STOT classification.

So let's look at this now with the premise that there will be a new endocrine disrupting classification. So what's actually happening if you ingest ethylene glycol?

Well firstly, there is a directly intoxicating effect in a similar manner to ethanol, directly intoxicating effect. That is not endocrine disrupting. That's a directly intoxicating effect, OK.

After that what happens is you get metabolites of the ethylene glycol.

And the first one is glycolic acid, which causes acidosis in the body. And I think that is potentially a STOT effect.

But in addition to that, another metabolite is oxalic acid. And the oxalic acid is what causes the urea crystals. So it's an oxalic calcium salt that forms.

And that has been shown in the renal cell to reduce the ability of the mitochondrial cell to respirate.

Janet Greenwood13:41

Right.

Alison13:42

And that is an inherited property in the cell, so that is shown in the next generation of the renal cell, which is why it causes the long term renal failure.

Janet Greenwood13:52

It's not something that the kidney cells can get over. Once they're damaged, it's passed on. The damage stays.

Alison14:00

Exactly. Yes.

So what you're seeing is you're seeing an adverse effect in the morphology growth and development in multiple generations. And that, I believe, comes under this endocrine disrupting property.

So what you're seeing here is what's currently handled by our STOT, which becomes a STOT and an endocrine disrupting property, potentially under the definition given.

Janet Greenwood14:33

Because it's weird, because to me, endocrine disruptors are things like the lymphatic system. You endocrine, rather, that's an endocrine system.

We're talking about things that control what goes on in the body. I mean, I hold my hand up here. I am not a biologist by any means, but it just seems that it's STOT.

STOT does seem to me to be and it's a STOT RE single. Umm single event, isn't it? (*with hindsight I should have said STOT SE!*)

Alison15:02

There is a lot of crossover here with STOT classifications and I think things that are already classified as STOT that have been classified as STOT for a very long time that have and it remember that if you go all the way back to CHIP.

You had some classifications that were either harmful as toxic with a slash and a route of exposure, so STOT was handled way back there in CHIP, and I think what you're looking at is some of these historical classifications that now maybe need to be reassessed to see if you're looking at an endocrine related adverse effect.

Where you're seeing something that's been well known, which now we need to look at the mechanism of toxicity.

Janet Greenwood15:51

I mean, at this point I have to say, if you're young and watching this, then toxicology is a growth area for jobs.

Alison15:58

Oh yes, very much so.

So I think there's going to be some confusion here.

And again, it comes back to this biological plausibility. So where one toxicologist might make a leap and say, "well, it seems plausible that this is, there's one study that suggests this might be the case". Another toxicologist just might go. "No, I don't think there's sufficient evidence or weight of evidence for this".

And we already see that happening because if you look at, like, the Japanese NITE classification list, they're already classifying a lot of substances with a STOT saying that the weight of evidence is sufficient. Whereas in Europe they're saying it's not sufficient, so we already have a range of toxicological opinions on things that have already have testing available.

Janet Greenwood16:46

We're chemists. We're just trying to classify things to the best of our ability and following the rules.

And what if this comes in in its current form? You're basically talking about toxicologists getting into a fist fight with each other, apart from things that have gone through reach registration because when you have a REACH registration, people have to agree the classification within the SIEF basically don't they.

So hopefully a lot for registered reach registered substance within the EU because this is there's no sign of it being brought into the UK yet, but we have to obviously be aware that that the way that GB-CLP is written is that everything that is in the EU CLP has to be at least considered. They can't ignore it. It's slightly different to what's happened with UK REACH where there isn't quite the same "shadowing" legally that we have to do (*with GB-CLP shadowing EU-CLP*).

But it's this thing of within the REACH dossier things will be hammered out there.

Where the real problems going to arise is things that have not got to REACH registration if it, like I say, it comes in in the current form.

Alison18:02

Now the mixtures. We do have a fairly simple threshold for classification, so category ones or threshold classification is 0.1%;The category two mixtures are threshold classification is going to be 1%. It's the same whether it's solid, liquid or gas.

What we are given are bridging principles.

Now it just states that bridging principles as per section one point 1.3 of CLP apply. Now if you go to the bridging principle section of CLP, each bridging principle itself states to which hazard categories it applies.

So presuming no modifications will be made to that section, and there's no modifications listed in this draft Commission regulation, that would suggest that we can apply:

- dilution
- batching
- substantially similar mixtures
- and the review where composition of a mixture has changed. So that's the slight banding permitted within concentration limits

So that's 4 bridging principles that we can use.

And it would rule out concentration of highly hazardous mixtures, interpolation within a hazard category, and also aerosol bridging principles. So those three would be ruled out.

The only other thing of note is that it does specifically state that studies that you're including for classification under health endocrine disrupting properties for health. You should also include the same studies under endocrine disrupting properties for the environment if they're relevant. And again, any study that you include for any other endpoint of CLP, if it's relevant included here too.

So you could end up using the same study all over the place and just reinterpreting it as relevant. So again, it really does point to the overlap in classification.

Janet Greenwood20:01

Yeah, yeah, absolutely. So before we wind up, is there any anything else that you want to add on this dog's dinner of endocrine disruptors?

Alison20:14

The only other thing I would point out is the transitional provisions.

After publication, so not from the date of the draft, but after publication, essentially you get 18 months for substances, 42 months if they're already on the market.

For mixtures 36 months or 60 months if they're already on the market.

That's a massive transition period that we're being granted here.

And part of me feels like it's because it's going to be so difficult to classify.

Not difficult to introduce new labelling, difficult to classify and to work out where the boundaries are and what crossover into another category and whatnot.

I really do think that this is really challenging when you line it up against STOT.

Janet Greenwood21:05

And the thing is, if we've got STOT already and we have long term effects in the aquatic environment, to all practical intents and purposes, what good is this doing? apart from creating jobs for toxicologists and eco toxicologists and lawyers?

I can see PBT, vPvB we know that that REACH has brought that in in effect, and it's a transfer. We can see that PMT and it's vPvB equivalent *(i.e vPvM)* that's coming out of biocides, it's coming out of plant protection products. So those are the easy bits,.

But this (*endocrine disruptors*) is just horrendous.

Alison21:47

It's gonna be a challenge.

You know, toxicologist are gonna be busy, I think is what I would say here. So it's called just about going to be very busy. There's a lot of crossover here with existing categories for classification. I think there's gonna be a lot of substances that are already classified, which may potentially fall into these categories.

Janet Greenwood21:55

Oh yeah.

Alison22:11

And then trying to work out what does and doesn't qualify. There's definitely gonna be some guesswork to a certain extent, because the science isn't necessarily there, and if you've already classified it as a STOT, would you really commission further work to identify the exact mechanism?

Janet Greenwood22:32

Oh, God, yeah. There's a there's a whole can of worms that around more animal testing.

Alison22:36

Yeah.

Janet Greenwood22:36

And even in the aquatic environment, if you're talking about fish, that they are also vertebrate animals.

So, so just to sort of summarize where we are, this is just at the discussion stage if people are.

Alison22:48
Open for consultation, yes, although they they have specifically called out in the fact that they have, in previous consultations, already addressed the following points.
Da da da da da.

So I don't think they're gonna be particularly open to discussion on some of these points.

Janet Greenwood23:06
I.
And again, that ties in with the fact that they're a bit nervous about the science, because I don't remember these consultations being particularly widespread.

I know here in the UK we are one step removed from it. But of course, if you sell into the EU then this will affect you. Clearly it will affect you. And if it goes to the UN, it will affect you as well.

But I think for me, in business terms, it's really important if you want to say something about the consultation, even if they claim they've already done it, get your get your information back to them as soon as possible. Say you're unhappy, say why you're unhappy, say why you think it's not going to work.

But for goodness sake, for everybody watching this, now, on the 21st of September 2022, this is not out yet.

Do not, repeat, **do not** take any actions on this.

Do not, **do not follow any regulations until they are actually brought in**, because we've seen it umpteen times before, there are changes before things come in.

And if you try and go too far in advance, you will run into problems.

So I think that our advice is:

This is coming. It's got the potential to be a big deal. Protest about it if you are involved, but otherwise sit on your hands. Don't get too involved in the rabbit hole and then, you know, maybe get a bit of popcorn. Watch and see on the political side?

But yeah, well, thank you very much, Ali. That's been really interesting and worrying and we've now got another meeting to go off into because it's that busy.

Alison24:41

Thanks everyone.

Janet Greenwood24:42

OK. Thank you. Bye.