



## Modernizing the Regulatory System for Biotechnology Products

### Third Public Meeting Transcript – Part One

University of California, Davis

Wednesday, March 30, 2016

## Table of Contents

How to Read this Transcript .....	2
Welcome - Dr. Josette Lewis, World Food Center, UC Davis .....	3
Opening Remarks and Agenda Review – Dr. Mike Firko, USDA APHIS Deputy Administrator, Biotechnology Regulatory Services .....	5
Modernizing the Regulatory System for Biotechnology Products: Background and Progress Made to Date — Dr. Robbie Barbero, Assistant Director for Biological Innovation White House Office of Science and Technology Policy .....	12
Regulation of Biotechnology Products—Clarifying Roles of and Coordination among USDA/APHIS, EPA, and FDA through a Discussion of Case Studies .....	26
Case Study: Hypothetical GE Corn with Pesticidal Properties.....	53
Case Study: Hypothetical Herbicide-Tolerant Canola .....	65
Case Studies Q&A Period for Products for Human and Animal Feed .....	70
Case Study: Hypothetical GE Rabbit .....	85
Case Study Q&A Hypothetical GE Rabbit .....	93
Case Study: Microbial Products for Industrial Applications .....	107
Case Study Q&A Microbial Products for Industrial Applications.....	119

## How to Read this Transcript

The text below each respective time stamp corresponds directly to the time of the recording file, which can be accessed at this URL:

<https://youtu.be/xsp4HxQ05RY>.

1  
00:00:22,878 --> 00:00:27,350  
>>APHIS Deputy Administrator, Biotechnology Regulatory Services  
Dr. Mike Firko>>  
Morning everyone, no, how about now?

2  
00:00:27,350 --> 00:00:28,680  
Got it?  
>> Yeah.

3  
00:00:28,680 --> 00:00:29,720  
>> Okay, let's get started,

4  
00:00:29,720 --> 00:00:34,300  
We're a couple of minutes late. We've got a very full agenda. Josette?

5  
00:00:36,360 --> 00:00:37,829  
>> Not a very formal introduction.

### Welcome - Dr. Josette Lewis, World Food Center, UC Davis

6  
00:00:40,880 --> 00:00:42,260  
>> Dr. Josette Lewis, World Food Center, UC Davis>> No point in being really formal.

7  
00:00:42,260 --> 00:00:45,095  
Hi I'm Josette Lewis with the World Food Center here at UC Davis.

8  
00:00:45,095 --> 00:00:49,650  
We're really pleased to be able to host this important discussion here today.

9  
00:00:49,650 --> 00:00:54,480  
As a university, one of our core businesses is doing research,

10  
00:00:54,480 --> 00:00:59,730  
and an important aspect of that research is to inform science based policy,

11  
00:00:59,730 --> 00:01:02,070  
an issue that of course we are here to talk about today.

12  
00:01:03,080 --> 00:01:07,740  
Another important avenue by which we contribute to society is through

13

00:01:07,740 --> 00:01:10,130

the translation of that research into technologies.

14

00:01:10,130 --> 00:01:15,540

And here at UC Davis we have a lot of relationships across the seed industry

15

00:01:15,540 --> 00:01:18,080

in our state of California and globally, and

16

00:01:18,080 --> 00:01:21,910

that's also an important industry that's impacted by our discussion here today.

17

00:01:23,340 --> 00:01:27,266

And lastly we're really pleased to have so many colleagues here from

18

00:01:27,266 --> 00:01:31,884

the Federal Government in Washington D.C. because we sit here in California.

19

00:01:31,884 --> 00:01:38,100

California and Washington are agriculture is called specialty crops by and

20

00:01:38,100 --> 00:01:43,150

large, yet we're the largest agricultural economy in the country and

21

00:01:43,150 --> 00:01:45,040

one of the top ten in the world.

22

00:01:45,040 --> 00:01:48,870

We produce over half of the fruits and vegetables in the US, so

23

00:01:48,870 --> 00:01:53,720

we play a pretty important role in the US diet and the quality of the US diet.

24

00:01:53,720 --> 00:01:58,020

But equally importantly we have one of the most diverse agricultural systems,

25

00:01:58,020 --> 00:02:02,520

not only in the types of crops that we produce, but also in the way in which we

26

00:02:02,520 --> 00:02:06,090

farm, the different types of farming practices and scales.

27

00:02:06,090 --> 00:02:10,000

And so this conversation here today is a really important opportunity for

28

00:02:11,250 --> 00:02:13,010

UC Davis to host you.

29

00:02:13,010 --> 00:02:16,260

And we're really pleased that so many people have turned out and to host our

30

00:02:16,260 --> 00:02:20,870

Federal agencies to participate in an important conversation that shapes all of

31

00:02:20,870 --> 00:02:24,710

these different aspects that are important to us as a research university.

32

00:02:24,710 --> 00:02:27,471

So I wanna thank you again for the opportunity to host this, and

33

00:02:27,471 --> 00:02:30,348

I will be here all day and look forward to hearing the discussion.

34

00:02:30,348 --> 00:02:33,128

Thank you very much.

## Opening Remarks and Agenda Review – Dr. Mike Firko, USDA APHIS Deputy Administrator, Biotechnology Regulatory Services

35

00:02:33,128 --> 00:02:40,060

>> [APPLAUSE]

>> Dr. Firko >>Is my lapel mic on?

36

00:02:41,110 --> 00:02:43,450

I'm a wanderer that's where I'm most comfortable so

37

00:02:43,450 --> 00:02:45,470

I'm gonna wander around a little bit.

38

00:02:45,470 --> 00:02:49,509

I'm Mike Firko, I'm with the US Department of Agriculture,

39

00:02:50,630 --> 00:02:55,880

the agency I work with is the animal and plant health inspection service, and

40

00:02:55,880 --> 00:03:01,000

I'm APHIS Deputy Administrator for Biotechnology Regulatory Services.

41

00:03:01,000 --> 00:03:06,920

So it's my shop in APHIS that has the piece of biotechnology regulation for

42

00:03:06,920 --> 00:03:07,580

USDA.

43

00:03:08,980 --> 00:03:10,470

I'd really like to thank everybody,

44

00:03:10,470 --> 00:03:15,190

this is a great turn out, it's more than what we were expecting, which is great.

45

00:03:15,190 --> 00:03:20,370

I'm looking at the list of folks who are registered, it's extremely diverse,

46

00:03:20,370 --> 00:03:25,510

we have folks from a broad range of groups, interests groups.

47

00:03:25,510 --> 00:03:30,720

That's great, we should have a lot of interesting discussion today.

48

00:03:30,720 --> 00:03:36,930

One of the core themes of this effort that Robbie Barbero

49

00:03:36,930 --> 00:03:40,620

with the Executive Office of the President and others in the Executive Office of

50

00:03:40,620 --> 00:03:44,949

the President are working towards is better communication in this space.

51

00:03:46,710 --> 00:03:52,160

So, I'm asking my colleagues today to think about communication,

52

00:03:52,160 --> 00:03:56,670

we tend to use jargon, we use not only scientific

53

00:03:56,670 --> 00:04:00,270

jargon sometimes, we use a lot of regulatory jargon.

54

00:04:01,410 --> 00:04:06,400

And as regulatory agencies we have to be very aware of how we're

55

00:04:06,400 --> 00:04:10,820

using the authority that has been granted to us by Congress,

56

00:04:10,820 --> 00:04:15,640

through legislation and then through regulations that we write.

57

00:04:16,910 --> 00:04:22,090

And we have to stay true to the authority that has been granted to us,

58

00:04:22,090 --> 00:04:26,920

we can only exercise authority that has been granted to us by Congress, and

59

00:04:26,920 --> 00:04:29,420

that we ourselves have written into regulations.

60

00:04:29,420 --> 00:04:33,010

So if you hear stuff from us that seems really weird, go ahead and

61

00:04:33,010 --> 00:04:36,950

ask the question, you know, why are you saying it that way?

62

00:04:38,390 --> 00:04:42,100

There's gonna be multiple opportunities today to talk about those things in

63

00:04:42,100 --> 00:04:48,300

the breakout groups, various question and answer sessions, and I look forward

64

00:04:48,300 --> 00:04:53,070

to the opportunity to help explain why we use such strange language sometimes.

65

00:04:54,840 --> 00:04:59,410

So looking at the agenda, we are doing some tweaking on the agenda because

66

00:04:59,410 --> 00:05:03,150

as I said this is a larger group than we anticipated.

67

00:05:03,150 --> 00:05:07,750

Primarily, it's a larger group in house,

68

00:05:07,750 --> 00:05:11,700

it's much larger than either of the two previous meetings in White Oak in

69

00:05:11,700 --> 00:05:15,470

Maryland, and also larger than the meeting that we had in Dallas.

70

00:05:17,390 --> 00:05:19,810

So, we'll start off with our

71

00:05:21,200 --> 00:05:25,300

next speaker will be Robbie Barbero from the White House Office of Science and

72

00:05:25,300 --> 00:05:30,195

Technology Policy, and then we'll have the speakers you see at the table.

73

00:05:30,195 --> 00:05:35,250

We'll be talking about the work that we do in this regulatory space,

74

00:05:36,560 --> 00:05:40,890

the case studies, three case studies in particular,

75

00:05:40,890 --> 00:05:44,860

then a short break, and then the breakout sessions.

76

00:05:44,860 --> 00:05:46,240

And, with the breakout sessions,

77

00:05:46,240 --> 00:05:51,530

that's primarily where we're going to have little bit of tweaking.

78

00:05:51,530 --> 00:05:55,720

Since we have many more people present than we expected,

79

00:05:55,720 --> 00:05:59,530

we're gonna have three locations where the breakouts will happen.

80

00:05:59,530 --> 00:06:00,940

One of them will be in this room,

81  
00:06:00,940 --> 00:06:04,950  
mostly in this section, people are still registering, and they're signing up  
for

82  
00:06:04,950 --> 00:06:10,300  
one of the three breakout sessions, so we'll see how those sizes work out.

83  
00:06:10,300 --> 00:06:14,640  
And then there are two break out rooms down the hall past the registration  
desk,

84  
00:06:14,640 --> 00:06:18,930  
so it'll be in those two rooms and probably in this section of this room.

85  
00:06:20,040 --> 00:06:24,830  
Now at the end of that break out listening session we had intended to have  
folks from

86  
00:06:24,830 --> 00:06:29,440  
each of those three groups come back here and do a verbal report out.

87  
00:06:29,440 --> 00:06:35,170  
We'd like to do other things, we'd like to leave time at the end for

88  
00:06:35,170 --> 00:06:37,180  
all of the public comments.

89  
00:06:37,180 --> 00:06:41,590  
So what we've decided to do is at the end of the break out listening sessions

90  
00:06:41,590 --> 00:06:46,430  
we'll go right into the public comment period and then the rapporteurs and

91  
00:06:46,430 --> 00:06:51,480  
the facilitators of those three breakout groups will work together over the  
next

92  
00:06:51,480 --> 00:06:54,400  
few weeks or so, and then all of the information

93  
00:06:54,400 --> 00:06:58,040  
from those break out listening groups will be posted on our websites.

94

00:06:58,040 --> 00:07:02,310

They'll be made public in a variety of different ways on the regs.gov

95

00:07:02,310 --> 00:07:05,060

area where this meeting has been located.

96

00:07:05,060 --> 00:07:07,320

You won't have that verbal report out today,

97

00:07:07,320 --> 00:07:12,370

but there will be a written report out made available in the near future, also,

98

00:07:12,370 --> 00:07:15,365

there will be a transcript of the proceedings.

99

00:07:15,365 --> 00:07:23,670

>> Unidentified speaker >> [INAUDIBLE] Are the public comments going to be recorded in any way?

100

00:07:23,670 --> 00:07:24,410

>> Dr. Firko >> Are they gonna be recorded?

101

00:07:24,410 --> 00:07:27,040

>> Unidentified speaker >> Recorded or submitted in one way.

102

00:07:27,040 --> 00:07:31,880

>> Dr. Firko >> They will be recorded, absolutely, the entire proceedings are being recorded.

103

00:07:31,880 --> 00:07:37,620

>> Unidentified speaker >> Will they be posted, or will the public comments be posted in one way [INAUDIBLE]

104

00:07:37,620 --> 00:07:38,500

>> Dr. Firko >> I believe they will all be-

105

00:07:38,500 --> 00:07:40,020

>> The whole meetings being transcribed.

106

00:07:40,020 --> 00:07:44,030

>> The whole meetings being transcribed so everything will be available.

107

00:07:44,030 --> 00:07:48,281

And in my experience in the previous two meetings you can

108

00:07:48,281 --> 00:07:50,909

submit written comments as well.

109

00:07:50,909 --> 00:07:55,453

With so many people, at this point we look like we have about 50 people

110

00:07:55,453 --> 00:07:57,898

registered to make public comments.

111

00:07:57,898 --> 00:07:59,974

We were thinking three minutes each.

112

00:07:59,974 --> 00:08:01,949

And if we give everybody three minutes,

113

00:08:01,949 --> 00:08:04,223

they're gonna be kicking us out of this room.

114

00:08:04,223 --> 00:08:07,079

Our contract goes until 3:00.

115

00:08:07,079 --> 00:08:09,982

So-

>> [INAUDIBLE]

116

00:08:09,982 --> 00:08:12,117

>> So we're going to give everybody

117

00:08:12,117 --> 00:08:17,073

a chance, everyone who is registered to make a comment will get a chance, but

118

00:08:17,073 --> 00:08:20,900

what that means is that we might have to be tough sometimes.

119

00:08:22,640 --> 00:08:26,890

There's a, you can't see it here but when you come up to make your public comment,

120  
00:08:26,890 --> 00:08:32,110  
there's about a 30 inch LCD screen right here that counts down from three minutes.

121  
00:08:32,110 --> 00:08:34,780  
And we're gonna have to stick to that because

122  
00:08:34,780 --> 00:08:38,290  
my primary value here today with the public comments is give everybody

123  
00:08:38,290 --> 00:08:41,049  
a chance to speak who has registered to speak.

124  
00:08:42,400 --> 00:08:45,510  
So I'm sorry if that means somebody gets cut a little short,

125  
00:08:45,510 --> 00:08:49,650  
but you have opportunities to submit any comments you want in writing.

126  
00:08:52,000 --> 00:08:54,460  
Any quick questions before I turn it over to Robbie?

127  
00:08:56,510 --> 00:08:57,010  
Thank you.

[Modernizing the Regulatory System for Biotechnology Products: Background and Progress Made to Date — Dr. Robbie Barbero, Assistant Director for Biological Innovation White House Office of Science and Technology Policy](#)

128  
00:09:03,126 --> 00:09:04,760  
>> Dr. Robbie Barbero, Assistant Director, Biological Innovation, Technology and Innovation Division, Executive Office of the President >> Great, thank you very much, Mike.

129  
00:09:04,760 --> 00:09:06,880  
Thank you everybody for being here.

130  
00:09:06,880 --> 00:09:12,154  
I would like to note that just as in a classroom full of students, the first

131  
00:09:12,154 --> 00:09:17,788  
row is almost totally empty, so even adults prefer not to sit in the front row.

132

00:09:17,788 --> 00:09:20,760

Just an interesting note on the sociology of people here.

133

00:09:20,760 --> 00:09:24,286

So, my name is Robbie Barbero, I work in the White House Office of Science and

134

00:09:24,286 --> 00:09:25,990

Technology Policy.

135

00:09:25,990 --> 00:09:29,580

And I'm going to provide a brief background on what we are doing and

136

00:09:29,580 --> 00:09:31,350

why we're doing it.

137

00:09:31,350 --> 00:09:34,706

And help you understand the process, and where we are in this process.

138

00:09:34,706 --> 00:09:38,576

So in 1986, The White House Office of Science and

139

00:09:38,576 --> 00:09:44,510

Technology Policy issued a policy document that described the relative roles and

140

00:09:44,510 --> 00:09:48,811

responsibilities, of the three primary agencies that had

141

00:09:48,811 --> 00:09:52,350

oversight over the products of biotechnology.

142

00:09:52,350 --> 00:09:54,799

That document was called the Coordinated Framework for

143

00:09:54,799 --> 00:09:57,130

the Regulation of Biotechnology.

144

00:09:57,130 --> 00:10:00,646

It did not endow new authorities onto those agencies,

145

00:10:00,646 --> 00:10:04,773

but what it did was it described how they would use their existing

146

00:10:04,773 --> 00:10:09,065

authorities in order to evaluate the products of biotechnology.

147

00:10:09,065 --> 00:10:12,620

In 1992, that document was updated.

148

00:10:12,620 --> 00:10:14,140

And then under this administration,

149

00:10:14,140 --> 00:10:17,550

and then the coordinated framework has not been updated since then.

150

00:10:17,550 --> 00:10:21,685

And so few years ago, this administration issued an Executive Order.

151

00:10:21,685 --> 00:10:26,630

That was not focused on bio technology called improving, and you know what,

152

00:10:26,630 --> 00:10:31,721

do we have the, can I have that clicker so I can get you to the right

[INAUDIBLE]

153

00:10:37,398 --> 00:10:39,840

So Mike left us behind when he was wandering.

154

00:10:39,840 --> 00:10:40,980

All right, here we are.

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00:10:40,980 --> 00:10:44,773

So this administration issued an Executive Order describing how all regulatory

156

00:10:44,773 --> 00:10:47,630

agencies could improve regulation and regulatory review.

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00:10:47,630 --> 00:10:53,455

And then last summer in July, the Executive Office of the President,

158

00:10:53,455 --> 00:10:58,689

which includes the Office of Science and Technology Policy and

159

00:10:58,689 --> 00:11:03,147

some of our other policy councils in the White House.

160

00:11:03,147 --> 00:11:07,701

Issued a memorandum drawing on the principles articulated in those three

161

00:11:07,701 --> 00:11:12,475

documents that are on this list ahead of it, essentially directing the EPA,

162

00:11:12,475 --> 00:11:13,943

the FDA, and the USDA,

163

00:11:13,943 --> 00:11:18,000

which are the three agencies that are sitting here at this table.

164

00:11:19,160 --> 00:11:21,512

To modernize the regulatory system for biotechnology products.

165

00:11:21,512 --> 00:11:26,146

And there are three primary tasks in that memorandum,

166

00:11:26,146 --> 00:11:29,477

and I will distill it down here for you.

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00:11:29,477 --> 00:11:33,853

And that memorandum is available on the website and in the docket, so

168

00:11:33,853 --> 00:11:35,442

you can access it there.

169

00:11:35,442 --> 00:11:38,650

Those three tasks are first to update the coordinated framework.

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00:11:38,650 --> 00:11:41,240

To clarify the current roles and

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00:11:41,240 --> 00:11:43,290

responsibilities of the regulatory agencies.

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00:11:43,290 --> 00:11:46,550

So that will mean that these agencies will say,

173  
00:11:46,550 --> 00:11:51,700  
here are the products over which each of them have regulatory oversight.

174  
00:11:51,700 --> 00:11:55,400  
The second was to commission and expert independent analysis

175  
00:11:55,400 --> 00:11:59,790  
of the future landscape of biotechnology products.

176  
00:11:59,790 --> 00:12:04,890  
And then the third was to issue a strategic plan that these

177  
00:12:04,890 --> 00:12:09,804  
three agencies would follow in order to make sure that the regulatory system  
for

178  
00:12:09,804 --> 00:12:13,807  
biotechnology products is well prepared for future biotechnology products.

179  
00:12:20,492 --> 00:12:24,086  
This memorandum further identified both the goals and

180  
00:12:24,086 --> 00:12:28,090  
laid out some guidance for those agencies to follow.

181  
00:12:28,090 --> 00:12:31,100  
And I will loosely read here off of this.

182  
00:12:31,100 --> 00:12:36,029  
So the essential guidance was that agencies should ensure that

183  
00:12:36,029 --> 00:12:39,292  
they regulate biotechnology products.

184  
00:12:39,292 --> 00:12:44,535  
And they should continually strive to improve predictability, increase

185  
00:12:44,535 --> 00:12:50,670  
efficiency, and reduce uncertainty in the regulatory processes and  
requirements.

186

00:12:50,670 --> 00:12:54,330

And that these improvements should maintain high standards

187

00:12:54,330 --> 00:12:56,722

based on the best available science.

188

00:12:56,722 --> 00:13:00,140

And that deliver appropriate health and environmental protection,

189

00:13:00,140 --> 00:13:04,300

establish transparent, coordinated, predictable, and efficient regulatory

190

00:13:04,300 --> 00:13:07,320

practices across these agencies with overlapping jurisdiction.

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00:13:07,320 --> 00:13:11,240

And part of what you will hear from us today when we discuss the case studies is

192

00:13:11,240 --> 00:13:14,505

how this coordination actually happens for actual products.

193

00:13:14,505 --> 00:13:18,978

And then to promote public confidence in the oversight of products of biotechnology

194

00:13:18,978 --> 00:13:21,750

through clear and transparent public engagement.

195

00:13:21,750 --> 00:13:25,910

And this is, to follow up on Mike's point, especially when we're discussing these

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00:13:25,910 --> 00:13:29,493

case studies, you will have an opportunity, once we've walked through

197

00:13:29,493 --> 00:13:33,000

each of the case studies, to ask questions for clarifying questions.

198

00:13:33,000 --> 00:13:37,370

We may not be able to get to all of those questions,

199

00:13:37,370 --> 00:13:42,170

but we'll certainly do our best to try to answer them.

200

00:13:42,170 --> 00:13:46,250

Now these are principles that guide these regulatory agencies to this day,

201

00:13:46,250 --> 00:13:50,920

they are drawn from the 1986 coordinated framework and from the 1992 update.

202

00:13:52,280 --> 00:13:57,057

In the interest of time, I will not go through all of these.

203

00:13:57,057 --> 00:14:02,815

But these slides will be made available to you on the website and

204

00:14:02,815 --> 00:14:05,540

on the docket on the back end.

205

00:14:05,540 --> 00:14:09,510

I think a few things here that are important to note is that this system is

206

00:14:09,510 --> 00:14:14,320

really intended to be based on science, and it is a risk based approach.

207

00:14:14,320 --> 00:14:17,500

So you will hear these agencies talk about these tenants

208

00:14:17,500 --> 00:14:19,970

as they're describing the authorities that they use and

209

00:14:19,970 --> 00:14:23,000

how they use them to ensure the safety of the products of biotechnology.

210

00:14:23,000 --> 00:14:28,402

There's a real strong emphasis also on coordination and

211

00:14:28,402 --> 00:14:35,730

working together whenever there are abutting or overlapping authorities.

212

00:14:35,730 --> 00:14:37,530

Okay, so where are we now in this process?

213

00:14:39,480 --> 00:14:43,910

Well, in July, as I said, the memorandum was issued, and shortly after that we did

214

00:14:43,910 --> 00:14:47,296

what every good bureaucracy does, we formed a working group.

215

00:14:47,296 --> 00:14:53,053

So this working group is called the Biotechnology Working Group,

216

00:14:53,053 --> 00:14:59,860

it's formed under an Emerging Technologies Interagency Policy Committee.

217

00:14:59,860 --> 00:15:03,405

And this working group has representatives from the executive offices

218

00:15:03,405 --> 00:15:06,960

of the President and each of the three agencies, EPA, FDA, and USDA.

219

00:15:08,630 --> 00:15:11,080

In October, this working group posted a request for

220

00:15:11,080 --> 00:15:14,982

information on the Federal Register with some description on what we were doing and

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00:15:14,982 --> 00:15:15,998

why we were doing it.

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00:15:15,998 --> 00:15:20,343

As well as some questions that were posed in order to help identify

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00:15:20,343 --> 00:15:24,846

information that would be useful to accomplish the three goals that

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00:15:24,846 --> 00:15:27,140

were laid out in that memorandum.

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00:15:28,270 --> 00:15:31,688

There are over 900 comments received on that.

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00:15:31,688 --> 00:15:36,740

And it was a very useful forum for gathering information.

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00:15:38,100 --> 00:15:43,916

During that open comment period, the first of the public meetings on this memorandum

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00:15:43,916 --> 00:15:49,084

was held at FDA, and we had over 300 people either watching on webcasts or

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00:15:49,084 --> 00:15:52,981

there in person, and received public comment at those.

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00:15:52,981 --> 00:15:57,482

The transcript from that meeting and all of the relevant materials are available

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00:15:57,482 --> 00:15:59,945

in the docket associated with this as well.

232

00:16:08,584 --> 00:16:11,023

Make sure that we're on the right slide, okay.

233

00:16:11,023 --> 00:16:15,585

In January, the National Academies of Sciences announced that they were

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00:16:15,585 --> 00:16:20,075

the entity that was going to be accomplishing the second of the tasks that

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00:16:20,075 --> 00:16:22,510

was identified in that memorandum.

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00:16:22,510 --> 00:16:27,040

So this is the the landscape analysis of future biotechnology products.

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00:16:27,040 --> 00:16:30,270

So the National Academies of Sciences announced that they were

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00:16:30,270 --> 00:16:31,710

initiating this study.

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00:16:31,710 --> 00:16:34,410

They're calling it the Future Biotechnology Products and

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00:16:34,410 --> 00:16:39,410

Opportunities to Enhance Capabilities of the Biotechnology Regulatory Systems.

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00:16:39,410 --> 00:16:43,657

And this study has four primary tasks.

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00:16:43,657 --> 00:16:46,153

The first is to identify major advances and

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00:16:46,153 --> 00:16:50,390

potential new types of biotech products over the next five to ten years.

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00:16:51,570 --> 00:16:55,400

To identify whether potential future products could pose different types of

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00:16:55,400 --> 00:16:57,470

risk, relative to existing products.

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00:16:59,480 --> 00:17:02,550

To identify areas in which the risk or lack of risks

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00:17:02,550 --> 00:17:07,070

associated with biotechnology products are well understood.

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00:17:07,070 --> 00:17:11,300

And then to extent that's possible identify what scientific capabilities,

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00:17:11,300 --> 00:17:15,350

tools, and expertise may be useful to the regulatory agencies

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00:17:15,350 --> 00:17:18,540

to support oversight of these potential future products of biotechnology.

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00:17:20,300 --> 00:17:23,270

The Academies have a website up for this now.

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00:17:23,270 --> 00:17:28,280

Just two weeks ago the Academies announced the provisional study committee.

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00:17:28,280 --> 00:17:31,310

And by provisional it just means that they are taking public comment in order to

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00:17:31,310 --> 00:17:34,390

identify potential conflicts of interest for this committee.

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00:17:34,390 --> 00:17:37,610

So you can go to this website and look at the committee, and

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00:17:37,610 --> 00:17:39,370

submit a comment on the committee.

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00:17:39,370 --> 00:17:43,350

And they also announced that the first public meeting on this study will be

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00:17:43,350 --> 00:17:47,795

happening on April 18th at the National Academy's building in Washington DC.

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00:17:51,764 --> 00:17:55,520

Now back to the work that this interagency working group has been doing.

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00:17:55,520 --> 00:18:01,219

So since November the interagency working group has reviewed all of the public

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00:18:01,219 --> 00:18:06,584

comments that were received in response to the request for information.

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00:18:06,584 --> 00:18:10,909

And using that information along with information gathered at

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00:18:10,909 --> 00:18:14,907

the public meetings is in the process of both drafting this

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00:18:14,907 --> 00:18:19,580

update to the coordinated framework and the long-term strategy.

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00:18:19,580 --> 00:18:22,860

The second public meeting was held at EPA on March 9th and

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00:18:22,860 --> 00:18:25,550

then today we are here for the third of the three public meetings.

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00:18:26,850 --> 00:18:31,260

And then this spring and summer timeline, the draft to the update of

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00:18:31,260 --> 00:18:34,420

the coordinated framework will be released and so will the long term strategy.

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00:18:34,420 --> 00:18:39,893

And it's important to note that that draft to the update to the coordinated framework

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00:18:39,893 --> 00:18:44,758

will be placed into the federal register and there will be an opportunity for

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00:18:44,758 --> 00:18:48,498

the public to comment on it, prior to it being finalized.

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00:18:48,498 --> 00:18:51,933

At that time all of the materials being associated with these three

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00:18:51,933 --> 00:18:54,093

public meetings will be in there as well.

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00:18:54,093 --> 00:18:57,295

And so if you are on the webcast or are here today and

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00:18:57,295 --> 00:19:01,652

would like to submit public comment in response to these meetings.

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00:19:01,652 --> 00:19:05,903

When the docket is opened and the update to the coordinated

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00:19:05,903 --> 00:19:10,587

framework is placed in there, that will be the time when you'll

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00:19:10,587 --> 00:19:15,380

have the opportunity to place comments in the federal register.

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00:19:15,380 --> 00:19:18,975

Okay, with that, let's get into some of the details now.

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00:19:18,975 --> 00:19:23,350

So as Mike said first we're going to walk through some case

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00:19:23,350 --> 00:19:26,130

studies of hypothetical products.

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00:19:26,130 --> 00:19:30,680

And these are case studies that were written by these agencies and

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00:19:30,680 --> 00:19:36,638

they're really intended to give you, to illustrate the roles and responsibilities

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00:19:36,638 --> 00:19:42,120

of these regulatory agencies, vis-a-vis various products of biotechnology.

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00:19:43,930 --> 00:19:47,060

Before we start into those case studies,

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00:19:47,060 --> 00:19:51,740

we thought that it would be helpful to give you a very high level snapshot of

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00:19:51,740 --> 00:19:54,680

the authorities that each of these agencies use.

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00:19:54,680 --> 00:19:59,990

And the protection goals that are associated with those authorities.

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00:19:59,990 --> 00:20:04,040

So when I say authority, that also could mean statute, so in this table here,

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00:20:04,040 --> 00:20:10,100

you'll see that there are three agencies that are listed and I believe, six

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00:20:10,100 --> 00:20:16,130

statutes that those agencies use in order to oversee products of biotechnology.

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00:20:16,130 --> 00:20:20,516

We'll give you a very high level overview of those, what each of the protection

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00:20:20,516 --> 00:20:25,111

goals associated with those are, and then start to talk through the case studies.

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00:20:25,111 --> 00:20:29,765

It's worth noting also that in addition to this table,

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00:20:29,765 --> 00:20:33,132

there is a table that's in the docket and

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00:20:33,132 --> 00:20:37,985

that is available on the website that is a much longer table

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00:20:37,985 --> 00:20:42,960

of authorities and oversight that you're welcome to use.

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00:20:42,960 --> 00:20:48,130

That information will be incorporated into the update to the coordinated framework

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00:20:48,130 --> 00:20:48,780

when it's released.

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00:20:48,780 --> 00:20:52,650

But that's another place where you can get a little bit finer grain detail on that.

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00:20:52,650 --> 00:20:55,719

All right, with that, let's go ahead and review some of these authorities.

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00:20:57,460 --> 00:20:58,037

Is this gonna work?

303

00:20:58,037 --> 00:21:00,220

We'll see if that microphone works.

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00:21:00,220 --> 00:21:00,780

Yeah.

## Regulation of Biotechnology Products—Clarifying Roles of and Coordination among USDA/APHIS, EPA, and FDA through a Discussion of Case Studies

305

00:21:00,780 --> 00:21:01,500

>> Dr. Neil Hoffman, USDA, APHIS, BRS >> Is this on?

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00:21:01,500 --> 00:21:02,340

Okay.

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00:21:02,340 --> 00:21:03,150

I'm Neil Hoffman.

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00:21:03,150 --> 00:21:07,390

I'm with the USDA, the Animal/Plant Health Inspection Service.

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00:21:07,390 --> 00:21:10,680

We have two programs that regulate biotechnology.

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00:21:10,680 --> 00:21:12,900

One is veterinary services and

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00:21:12,900 --> 00:21:17,650

they regulate under the authority of the Animal Health Protection Act.

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00:21:17,650 --> 00:21:22,220

And this shows up here their protection goal

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00:21:22,220 --> 00:21:27,270

is to protect livestock from animal pests and diseases.

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00:21:27,270 --> 00:21:32,490

And on the plant side we have Biotechnology Regulatory Services,

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00:21:32,490 --> 00:21:37,740

which uses the authority under the Plant Protection Act to protect agricultural

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00:21:37,740 --> 00:21:42,410

plants and agriculturally important natural resources from damage

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00:21:42,410 --> 00:21:47,420

caused by organisms that pose plant, pest or noxious weed risks.

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00:21:48,680 --> 00:21:52,730

I will turn this now over to my colleague from the EPA, Mike Mendelsohn.

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00:21:57,200 --> 00:21:59,890

>> Mike Mendelsohn, Senior Regulatory Specialist, Microbial Pesticides and Plant Incorporated Protectants, Office of Pesticide Protectants, Environmental Protection Agency >> Good morning, this is Mike Mendelsohn, and

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00:21:59,890 --> 00:22:03,520

I'm gonna talk about the pesticide part of EPA.

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00:22:03,520 --> 00:22:08,030

My colleague Mark Segal will talk about TSCA.

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00:22:08,030 --> 00:22:12,460

Under the Federal Insecticide, Fungicide, and Rodenticide Act, our protection goals

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00:22:12,460 --> 00:22:17,080

are to eliminate unreasonable adverse effects upon man and the environment.

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00:22:18,350 --> 00:22:23,193

And for environmental and occupational risks, this involves comparing economics,

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00:22:23,193 --> 00:22:27,582

social and environmental risks and benefits associated with pesticide use.

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00:22:27,582 --> 00:22:32,406

For dietary residential human health effects the sole standard is the safety of

327

00:22:32,406 --> 00:22:33,130

exposure.

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00:22:34,740 --> 00:22:37,800

And then in addition to FIFR, which is the licensing statute,

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00:22:37,800 --> 00:22:43,680

the pesticide registration statute, we have the Food, Drug, and Cosmetic Act.

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00:22:43,680 --> 00:22:48,497

And under that act, the protection goes to ensure dietary exposure

331

00:22:48,497 --> 00:22:52,396

to pesticide chemical residues in or on food are safe.

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00:22:52,396 --> 00:22:56,997

I'll turn it over to Mark.

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00:22:56,997 --> 00:23:01,668

>> Mark Segal, Office of Pollution and Prevention, Environmental Protection Agency >>Hi, I'm Mark Segal from the Office of Pollution and

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00:23:01,668 --> 00:23:06,764

Prevention and Toxics at EPA and statute that we work with

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00:23:06,764 --> 00:23:12,940

is the Toxic Substances Control Act, as Mike referred to it, TSCA.

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00:23:14,900 --> 00:23:20,354

Our protection goals as indicated deal with ensuring

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00:23:20,354 --> 00:23:25,565

that all aspects of commercialization of chemical

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00:23:25,565 --> 00:23:30,170

substances, manufacturing, processes,

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00:23:30,170 --> 00:23:35,396

distribution, and commerce use, disposal etc.

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00:23:35,396 --> 00:23:40,518

That with any combination of these activities does not

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00:23:40,518 --> 00:23:47,100

present an unreasonable risk of injury to health or the environment.

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00:23:49,360 --> 00:23:53,270

And I guess with that I'll turn it over to Jason.

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00:23:57,676 --> 00:24:01,879

>> Jason Dietz, Center for Food Safety and Applied Nutrition, Food and Drug Administration >> Good morning.

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00:24:01,879 --> 00:24:03,667

Good morning, my name is Jason Dietz.

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00:24:03,667 --> 00:24:07,316

I'm with the FDA's Center for Food Safety and Applied Nutrition.

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00:24:07,316 --> 00:24:13,990

FDA regulates approximately 20 to 25 cents of every consumer dollar spent.

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00:24:13,990 --> 00:24:19,200

The statutes that we use to regulate those products include the Federal Food Drug and

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00:24:19,200 --> 00:24:22,390

Cosmetic Act, as you've heard a little bit about from EPA,

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00:24:22,390 --> 00:24:25,710

as well as the Public Health Service Act.

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00:24:25,710 --> 00:24:30,490

And in terms of our protection goals for food, we certainly ensure that food, and

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00:24:30,490 --> 00:24:33,820

that includes food for humans as well as food for animals,

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00:24:33,820 --> 00:24:36,630

whether it be domestic, companion animals,

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00:24:36,630 --> 00:24:40,867

or production animals, that that food is safe, sanitary, and properly labeled.

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00:24:40,867 --> 00:24:45,720

We also ensure that drugs for humans and animals are safe and effective,

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00:24:45,720 --> 00:24:49,010

as well as biologics for humans.

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00:24:49,010 --> 00:24:53,071

We also ensure the safety and effectiveness of medical devices for

357

00:24:53,071 --> 00:24:54,340  
humans.

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00:24:54,340 --> 00:24:58,160  
We also regulate cosmetics many of you all may use.

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00:24:58,160 --> 00:25:02,840  
We must ensure that cosmetics are safe and lawful and properly labelled.

360

00:25:02,840 --> 00:25:07,908  
And we also regulate tobacco products.

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00:25:07,908 --> 00:25:09,743  
Thank you.

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00:25:09,743 --> 00:25:11,125  
>> Dr. Barbero >> Okay, great, thank you everybody.

363

00:25:11,125 --> 00:25:14,778  
So just go through a little bit of an overview,

364

00:25:14,778 --> 00:25:20,404  
some of the data requirements that are associated with the authorities

365

00:25:20,404 --> 00:25:25,278  
that we just talked about, after we go through this overview,

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00:25:25,278 --> 00:25:30,083  
then we'll walk through some of the specific case studies.

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00:25:30,083 --> 00:25:31,844  
>> Dr. Hoffman >> And will you be advancing the slides?

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00:25:31,844 --> 00:25:33,850  
>> Dr. Barbero >> I'll do the slides for you Neil, yep.

369

00:25:33,850 --> 00:25:39,228  
>> Dr. Hoffman >> So one thing we wanted to distinguish is between containment and confinement.

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00:25:39,228 --> 00:25:40,700  
APHIS regulates, and

371  
00:25:40,700 --> 00:25:45,770  
when the APHIS regulates biotechnology, it's through a permitting type system.

372  
00:25:45,770 --> 00:25:51,440  
And I just wanted to clarify that we have regulated confined field trials.

373  
00:25:51,440 --> 00:25:56,790  
We regulate movement, we regulate what is outside of enclosures,

374  
00:25:56,790 --> 00:25:59,880  
but we actually don't regulate inside an enclosure.

375  
00:25:59,880 --> 00:26:03,320  
So a containment system is not regulated by APHIS.

376  
00:26:03,320 --> 00:26:06,610  
The idea of by containment,

377  
00:26:06,610 --> 00:26:10,770  
we refer to things like greenhouses or growth chambers.

378  
00:26:10,770 --> 00:26:15,120  
The ideas prevent exposure of those GE plants to the environment, and

379  
00:26:15,120 --> 00:26:17,570  
the probability of release should be near zero.

380  
00:26:17,570 --> 00:26:21,559  
In a confinement, it's like an outdoor field trial, and

381  
00:26:21,559 --> 00:26:26,670  
there we're trying to ensure that GE plants do not persist in the environment.

382  
00:26:27,840 --> 00:26:30,450  
Next slide, please.

383  
00:26:30,450 --> 00:26:35,480  
So to show a visual, this is a greenhouse with corn growing in a greenhouse.

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00:26:35,480 --> 00:26:41,890

And very often in the early stages, much of the research is done in

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00:26:41,890 --> 00:26:46,340

contained facilities, such as a greenhouse like this, or in growth chambers.

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00:26:46,340 --> 00:26:48,250

And again, this would not be regulated.

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00:26:48,250 --> 00:26:52,900

The next slide, please.

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00:26:52,900 --> 00:26:58,200

If a GE organism was shipped from one facility to another,

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00:26:58,200 --> 00:27:02,468

that movement would require some sort of an authorization.

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00:27:02,468 --> 00:27:06,850

In contrast, our confined field trials,

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00:27:06,850 --> 00:27:11,630

the idea is that there are certain conditions imposed on

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00:27:11,630 --> 00:27:16,870

those field trials to prevent the plant persistence.

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00:27:16,870 --> 00:27:22,506

And some of these requirements that are imposed would

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00:27:22,506 --> 00:27:27,840

be to say maintain an appropriate separation distance

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00:27:27,840 --> 00:27:33,140

from a nearby plant, plants that are asexually compatible.

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00:27:33,140 --> 00:27:37,460

And you can see here that there's some area that's

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00:27:39,340 --> 00:27:43,030

foul around the plants, so one can look for escapes.

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00:27:43,030 --> 00:27:43,880

If you can hit, yeah.

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00:27:45,120 --> 00:27:51,110

There are other requirements that have to do with cleaning equipment so that

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00:27:52,800 --> 00:27:57,140

plant material from that field trial is not left in planters,

401

00:27:57,140 --> 00:28:03,090

which are then moved off site and might spread the organism.

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00:28:03,090 --> 00:28:07,280

That there are restrictions on what can be grown in those fields the next

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00:28:07,280 --> 00:28:11,376

growing season, there are restrictions on monitoring for volunteer plants, and

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00:28:11,376 --> 00:28:17,550

there are restrictions to look for nearby sexually compatible plants.

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00:28:17,550 --> 00:28:19,511

In the case where there are wild relatives,

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00:28:19,511 --> 00:28:23,890

that those would need to be controlled, or that plant would not be allowed to flower,

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00:28:25,150 --> 00:28:30,120

and that the GE seed from the test is not used for human or animal food.

408

00:28:30,120 --> 00:28:30,959

Next slide, please.

409

00:28:33,470 --> 00:28:37,130

So when one is doing confined field trials,

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00:28:37,130 --> 00:28:41,680

some of the considerations in terms of what kinds of conditions are used,

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00:28:41,680 --> 00:28:45,980 you ask, is the crop out-crossing or self-pollinating?

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00:28:45,980 --> 00:28:48,120

Is it weedy or invasive?

413

00:28:48,120 --> 00:28:50,790

Are there wild or invasive relatives?

414

00:28:50,790 --> 00:28:55,740

Can the plant or offspring persists after the test is over, and

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00:28:55,740 --> 00:28:59,170

would the traits be expected to change the plant's weediness,

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00:28:59,170 --> 00:29:06,900

invasive, or reproductive biology?

417

00:29:06,900 --> 00:29:10,670

Again, these are all considerations about what kind of

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00:29:10,670 --> 00:29:14,890

requirements should be used to help keep that field trail confined.

419

00:29:14,890 --> 00:29:16,510

Next slide, please.

420

00:29:17,510 --> 00:29:23,710

Then, we have a process where a developer of a biotech crop,

421

00:29:23,710 --> 00:29:29,400

or a biotech organism, can petition for non-regulated status.

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00:29:29,400 --> 00:29:33,224

In that situation, if non-regulated status is granted,

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00:29:33,224 --> 00:29:36,850

then permits are no longer required for the authorization for

424

00:29:36,850 --> 00:29:42,340

the movements, the interstate movement, importation, or environmental release.

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00:29:42,340 --> 00:29:46,770

And in those kind of considerations, we look at the crop biology and the taxonomy.

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00:29:46,770 --> 00:29:54,330

Are there genotypic differences between the GE crop and non-GE crop?

427

00:29:54,330 --> 00:29:57,020

Are there phenotypic differences?

428

00:29:57,020 --> 00:30:00,930

We look at the field test reports and what data was collected during those reports

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00:30:00,930 --> 00:30:03,400

and any other relevant experimental data,

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00:30:03,400 --> 00:30:08,290

publications, and data upon which to base a determination.

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00:30:08,290 --> 00:30:08,900

Next slide, please.

432

00:30:10,760 --> 00:30:14,540

There are two kinds of evaluations we do for

433

00:30:14,540 --> 00:30:17,170

a petition process for non-regulated status.

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00:30:17,170 --> 00:30:20,950

One is we call it a Plant Pest Risk Assessment.

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00:30:20,950 --> 00:30:24,990

Again, we only talked about our protection goals.

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00:30:24,990 --> 00:30:29,070

Our protection goals are based on not just reader plant pest authority.

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00:30:29,070 --> 00:30:34,210

And if ever regulations really are only based on that plant pest authority,

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00:30:34,210 --> 00:30:37,790

we do a plant pest risk assessment to determine whether the GE

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00:30:37,790 --> 00:30:40,630

organism poses a risk as a plant pest.

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00:30:40,630 --> 00:30:44,490

And if not, we must deregulate it.

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00:30:44,490 --> 00:30:46,940

>> Dr. Barbero >> And Neil, can I interrupt you here just to clarify for folks here?

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00:30:46,940 --> 00:30:51,190

So you said, you just said your regulations, you said authority and

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00:30:51,190 --> 00:30:51,740

regulations.

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00:30:51,740 --> 00:30:55,005

So you can give a little explanation of what the difference is between those two?

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00:30:55,005 --> 00:30:59,660

>> Dr. Hoffman >> So we used, the Plant Pest Act has authority, and

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00:30:59,660 --> 00:31:05,460

the Plant Pest Act has authority to look at both plant pests and noxious weeds.

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00:31:05,460 --> 00:31:09,821

Our regulations were put together prior to the Plant Pest Act,

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00:31:09,821 --> 00:31:14,757

which was cobbled together from a number of acts, and we never codified

449

00:31:14,757 --> 00:31:19,548

the noxious weed provision of the Plant Pest Act in the regulations.

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00:31:19,548 --> 00:31:20,987

And that is one of the things.

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00:31:20,987 --> 00:31:25,050

You may know that BRS is revising its regulations.

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00:31:25,050 --> 00:31:30,195

And one of the objectives for revising the regulation is to

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00:31:30,195 --> 00:31:35,340

consider whether to codify the Noxious Weeds Authority or

454

00:31:35,340 --> 00:31:41,030

the Plant Pest Act into the new biotech regulations, CFR 73.

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00:31:41,030 --> 00:31:46,236

>> Dr. Barbero >> So Congress writes the statutes, and the agency writes the regulations.

456

00:31:46,236 --> 00:31:47,240

>> Dr. Hoffman >> That's correct.

457

00:31:47,240 --> 00:31:52,708

Sorry about that, I wasn't sure what you all needed to hear about that.

458

00:31:52,708 --> 00:31:58,240

The other evaluation that APHIS does at the time of considering a petition for

459

00:31:58,240 --> 00:32:02,839

non-regulated status is to do an environmental assessment or

460

00:32:02,839 --> 00:32:05,860

environmental impact statement.

461

00:32:05,860 --> 00:32:11,330

So we have NEPA obligations, and generally, NEPA obligation,

462

00:32:11,330 --> 00:32:16,340

if it's not a significant action, would be an environmental assessment,

463

00:32:16,340 --> 00:32:20,110

or if it was a significant one and that's a term of art, but

464

00:32:20,110 --> 00:32:23,840

I won't go into, is to do an environmental impact statement.

465

00:32:23,840 --> 00:32:27,140

And lastly, I'll just describe what are some of the components of a plant

466

00:32:27,140 --> 00:32:28,190

pest risk assessment.

467

00:32:29,360 --> 00:32:34,610

Again, our authority is to look at the plant pest potential,

468

00:32:34,610 --> 00:32:39,210

and so we consider whether the modification to this

469

00:32:39,210 --> 00:32:44,280

GE plant will create pest or disease problems for agriculture.

470

00:32:44,280 --> 00:32:46,670

We also consider whether it will become a weed,

471

00:32:46,670 --> 00:32:50,560

whether it will increase the weediness of sexually compatible plants,

472

00:32:50,560 --> 00:32:53,920

whether it will harm non-target organisms.

473

00:32:53,920 --> 00:32:56,488

Example, beneficial or endangered species.

474

00:32:56,488 --> 00:32:59,870

Whether it will affect agricultural practices,

475

00:32:59,870 --> 00:33:03,960

in a way, which could create disease and pest problems, and whether it

476

00:33:03,960 --> 00:33:09,480

can transmit the genes to organisms with which it does not normally interbreed.

477

00:33:09,480 --> 00:33:11,790

>> Dr. Barbero >> And I'd just like to highlight this slide.

478

00:33:11,790 --> 00:33:16,030

For those of you who might ask the question, what information

479

00:33:16,030 --> 00:33:21,270

would APHIS want from me in order to engage in a process?

480

00:33:21,270 --> 00:33:26,600

This is a good summary slide for you to look at, cuz these are the kinds

481

00:33:26,600 --> 00:33:30,575

of questions or the type of information that are important to APHIS in order for

482

00:33:30,575 --> 00:33:34,180

APHIS to make a determination about whether there is a plant pest risk.

483

00:33:34,180 --> 00:33:34,957

>> Dr. Hoffman >> Thanks, Robbie.

484

00:33:39,694 --> 00:33:41,782

>> Dr. Barbero >> Okay, Mark.

485

00:33:41,782 --> 00:33:45,341

So now, we are switching to a different agency and

486

00:33:45,341 --> 00:33:47,897

a different statutory authority.

487

00:33:47,897 --> 00:33:52,750

And this slide is a parallel to the slide just previous to it, so

488

00:33:52,750 --> 00:33:58,264

Mark will talk about if you are developing a different type of product.

489

00:33:58,264 --> 00:34:00,818

So we're not talking about crops here.

490

00:34:00,818 --> 00:34:03,206

We're talking about microorganisms,

491

00:34:03,206 --> 00:34:08,119

the kind of information that is important to EPA as they use their authority granted

492

00:34:08,119 --> 00:34:10,940

to them under the Toxic Substance Control Act.

493

00:34:13,130 --> 00:34:17,465

>> Dr. Mark Segal, Senior Microbiologist, Office of Pollution Prevention and  
Toxics, Environmental Protection Agency >> All right, so to start with, I have  
to make sure you understand that

494

00:34:17,465 --> 00:34:22,769

TSCA does not have explicit data requirement for submissions

495

00:34:22,769 --> 00:34:27,880

that receive pre-manufacturing oversight, which is what we'll be talking about.

496

00:34:27,880 --> 00:34:31,600

Rather, TSCA requires submitters to provide

497

00:34:31,600 --> 00:34:36,060

EPA with whatever data that are relevant to our risk assessments,

498

00:34:36,060 --> 00:34:40,710

that they may have in their possession, or that are reasonably ascertainable by  
them.

499

00:34:41,770 --> 00:34:42,660

So that's pretty broad.

500

00:34:45,360 --> 00:34:49,595

EPA, therefore, has provided guidance to assist

501

00:34:49,595 --> 00:34:55,650

submitters as well as to help ensure that EPA gets the data that it needs.

502

00:34:55,650 --> 00:34:59,790

The guidance is what we call our Points to Consider. (Points to Consider in

503

00:34:59,790 --> 00:35:05,558

the Preparation of TSCA Biotechnology Submissions for Microorganisms).

504

00:35:05,558 --> 00:35:12,019

>> Unidentified Speaker >> [INAUDIBLE]

>> Dr. Segal >> Okay,

505

00:35:12,019 --> 00:35:16,777

so I guess I was gonna get to it, but I'll do it right now.

506

00:35:16,777 --> 00:35:19,200

>> Dr. Barbero >> And this is all background information.

507

00:35:19,200 --> 00:35:23,000

When we walk through the case studies, you'll get some of these explained to you,

508

00:35:23,000 --> 00:35:27,730

but this is background information that's generic across many of the case studies,

509

00:35:27,730 --> 00:35:29,095

and we wanted to provide it to you.

510

00:35:29,095 --> 00:35:33,480

We recognize that it is nearly impossible to absorb all of these

511

00:35:33,480 --> 00:35:38,030

the first time through, but we'll do our best to reiterate it and

512

00:35:38,030 --> 00:35:41,276

talk through it, but that is a good question.

513

00:35:41,276 --> 00:35:45,047

>> Dr. Segal >> So on another slide--- and later on, they'll be explained---

514

00:35:45,047 --> 00:35:48,203

But a TERA, T-E-R-A,

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00:35:48,203 --> 00:35:53,798

is a TSCA Experimental Release Application,

516

00:35:53,798 --> 00:35:59,979

an MCAN, Microbial Commercial Activity Notice.

517

00:35:59,979 --> 00:36:04,422

So I will get to those exactly in just a bit.

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00:36:04,422 --> 00:36:09,246

So anyway, this Points to Consider document is

519

00:36:09,246 --> 00:36:14,894

intended to provide assistance to those who come to us and

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00:36:14,894 --> 00:36:21,760

make sure that, as I said, that we get the data that we need.

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00:36:21,760 --> 00:36:27,800

So it's expected to be a broad presentation of

522

00:36:27,800 --> 00:36:33,070

the range of data categories that might be relevant

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00:36:33,070 --> 00:36:38,950

to any risk assessment that we might encounter.

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00:36:38,950 --> 00:36:43,992

Therefore, we don't expect every submitter to have

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00:36:43,992 --> 00:36:48,698

to provide us with every piece of every category of

526

00:36:48,698 --> 00:36:54,301

information that is provided within our Points to Consider

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00:36:54,301 --> 00:36:59,363

since we have to deal with such a broad range of cases.

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00:36:59,363 --> 00:37:05,490

We expect a submitter to go through the list of information that we provide and

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00:37:05,490 --> 00:37:10,769

think about what's relevant to their particular case that points

530

00:37:10,769 --> 00:37:16,447

to consider best, to considerations that we're expecting them to do.

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00:37:16,447 --> 00:37:23,773

To go through this, look at the data types that are relevant.

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00:37:23,773 --> 00:37:27,827

And we then provide, within our Points to Consider,

533

00:37:27,827 --> 00:37:30,709

guidance on how to present that data,

534

00:37:30,709 --> 00:37:35,410

some ways to collect the data so that we have it properly done.

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00:37:36,920 --> 00:37:41,220

So what this slide does is illustrate the categories of

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00:37:41,220 --> 00:37:46,800

information that are provided within this document.

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00:37:46,800 --> 00:37:51,960

The very first thing we need to know is what is the product identity,

538

00:37:51,960 --> 00:37:55,380

what is the organism that you're working with.

539

00:37:55,380 --> 00:38:01,103

We need to understand how this organism may be related to other similar

540

00:38:01,103 --> 00:38:07,408

organisms for which we might be able to gather additional data besides that,

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00:38:07,408 --> 00:38:11,376

which is provided by the submitter. [CROSSTALK]

>> Dr. Barbero >> And Mark, I'm just gonna remind you,

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00:38:11,376 --> 00:38:14,188

we're already a little over time, so let's briefly run through this and-

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00:38:14,188 --> 00:38:16,040

>> Dr. Segal >> Okay, well, so quickly,

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00:38:16,040 --> 00:38:21,758

we need product identification, we need to know how the organism was put together,

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00:38:21,758 --> 00:38:26,207

we need to know the obvious things as everybody has talked about.

546

00:38:26,207 --> 00:38:27,772

Does it affect human health?

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00:38:27,772 --> 00:38:30,370

Does it affect the environment?

548

00:38:30,370 --> 00:38:34,430

What are the explicit effects that might be considered?

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00:38:35,860 --> 00:38:38,620

We are also concerned with worker exposure, so

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00:38:38,620 --> 00:38:43,030

we look at releases from the worker environment and

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00:38:43,030 --> 00:38:46,710

the use environment and exposure to the general population.

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00:38:49,000 --> 00:38:53,690

For the TERA, the experimental release application,

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00:38:53,690 --> 00:38:58,210

we're gonna look at some specifics of the site, things like monitoring,

554

00:38:59,290 --> 00:39:03,000

issues that are unique to that set of experiments.

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00:39:03,000 --> 00:39:08,126

Whereas for the MCAN, we look at the entire broad range of plausible uses

556

00:39:08,126 --> 00:39:13,090

of the microorganism beyond what those that maybe

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00:39:13,090 --> 00:39:18,760

the submitter may have considered they intend to use,

558

00:39:18,760 --> 00:39:23,300

because somebody else may want to use the same organism for a different purpose.

559

00:39:23,300 --> 00:39:24,190

And I think that's it.

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00:39:24,190 --> 00:39:28,420

>> Dr. Barbero >> All right And we recognize that this is a lot of information.

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00:39:28,420 --> 00:39:32,155

There is much more detail available in the lengths that are in these slides.

562

00:39:32,155 --> 00:39:34,394

And certainly, at any point,

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00:39:34,394 --> 00:39:39,490

you can also reach out to these agencies and discuss the information.

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00:39:39,490 --> 00:39:43,465

And in the case studies that have been handed out to you as well,

565

00:39:43,465 --> 00:39:47,894

some of these information is illustrated in a more practical manner.

566

00:39:47,894 --> 00:39:49,542

Okay, Mike.

567

00:39:49,542 --> 00:39:50,109

>> Mike Mendelsohn >> Okay.

568

00:39:50,109 --> 00:39:56,049

>> Dr. Barbero >> Okay, so now we are not talking About the Toxic Substances Control Act any more.

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00:39:56,049 --> 00:39:59,090

Now we're switching over to a different part of EPA.

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00:39:59,090 --> 00:40:03,050

>> Mike Mendelsohn >> Right, so in the Office of Pesticide Programs, we focus on

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00:40:03,050 --> 00:40:07,906

the Federal Insecticide, Fungicide, and Rodenticide Act or FIFRA and FFDCA or

572

00:40:07,906 --> 00:40:12,180  
FD&C, the Food, Drug, and Cosmetic Act.

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00:40:12,180 --> 00:40:17,830  
And what these data that we require are used

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00:40:17,830 --> 00:40:22,990  
to do is to help us make the regulatory decision for licensing a pesticide.

575

00:40:22,990 --> 00:40:27,691  
That there are no unreasonable adverse effects to man or

576

00:40:27,691 --> 00:40:32,599  
the environment, and also the dietary risk assessment.

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00:40:32,599 --> 00:40:37,072  
Basically, there's a reasonable certainty of no harm from the residue of

578

00:40:37,072 --> 00:40:38,706  
the pesticide in the food.

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00:40:38,706 --> 00:40:45,670  
And so those are the two, assessments that are made, the regulatory  
assessments.

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00:40:45,670 --> 00:40:50,600  
And to support those we require this data to perform risk assessments.

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00:40:50,600 --> 00:40:54,630  
So this is briefly for plant-incorporated protectants.

582

00:40:54,630 --> 00:40:58,690  
We also look at genetically engineered microbes that have pesticidal  
properties.

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00:40:58,690 --> 00:41:02,610  
But I'm gonna talk primarily today about the plant-incorporated protectants, or

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00:41:02,610 --> 00:41:03,170  
PIPs.

585

00:41:04,790 --> 00:41:08,050

So the first thing we'd look at is how to characterize the PIP,

586

00:41:08,050 --> 00:41:11,550

and-

>> Dr. Barbero >> And a plant-incorporated protectant is?

587

00:41:11,550 --> 00:41:12,173

>> Mike Mendelsohn >> Thank you Robbie.

588

00:41:12,173 --> 00:41:16,821

[LAUGH] Okay, so the way we define a plant-incorporated protectant,

589

00:41:16,821 --> 00:41:21,393

it's the genetic material necessary for production of a pesticidal

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00:41:21,393 --> 00:41:25,276

substance as well as a pesticidal substance in the plant.

591

00:41:25,276 --> 00:41:28,800

So in short, it is not the plant.

592

00:41:28,800 --> 00:41:30,731

But it is the pesticidal substance and

593

00:41:30,731 --> 00:41:34,908

the genetic material necessary to produce that pesticidal substance in a plant.

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00:41:38,058 --> 00:41:43,145

So in assessing the risk for that to make those two findings,

595

00:41:43,145 --> 00:41:48,948

we look at how we characterize the PIP by the transformation system.

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00:41:48,948 --> 00:41:51,251

Characterization of the DNA inserted into the plant.

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00:41:51,251 --> 00:41:53,435

We look at inheritance and

598

00:41:53,435 --> 00:41:57,610

stability of the genetic insertion after transformation.

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00:41:57,610 --> 00:42:00,320

And we look at the protein characterization expression of

600

00:42:00,320 --> 00:42:01,460

the pesticidal substance.

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00:42:01,460 --> 00:42:05,447

Of course, for different types of PIPs, this will be tweaked somewhat.

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00:42:06,820 --> 00:42:11,380

To look at the human health effects of PIPs, we mainly look at toxicity and

603

00:42:11,380 --> 00:42:12,250

allergenicity.

604

00:42:14,860 --> 00:42:17,970

We require in vitro digestibility assay to look at allergenicity.

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00:42:19,050 --> 00:42:24,990

We also require amino acid homology to look at both toxin and

606

00:42:24,990 --> 00:42:26,700

allergen possibilities.

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00:42:26,700 --> 00:42:31,540

We look at heat stability and we require an acute oral toxicity study.

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00:42:31,540 --> 00:42:35,520

Again, these types of data are used to assess the human health risk.

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00:42:36,690 --> 00:42:40,720

And lastly, I'd like to talk about how we assess environmental effects of PIPs.

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00:42:41,920 --> 00:42:46,770

Again, we look at what's the pesticidal substances being produced in the plant.

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00:42:46,770 --> 00:42:51,290

We look at environment fate of the pesticidal substance.

612

00:42:51,290 --> 00:42:56,560

How long it persists in the environment, in the leaf tissue, in the soil, etc.

613

00:42:56,560 --> 00:43:02,180

We look at gene flow, how that genetic material can pass in the environment.

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00:43:02,180 --> 00:43:06,050

And we look at non-target effects of the pesticidal substance.

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00:43:06,050 --> 00:43:09,778

So this slide is basically an entire presentation orally, so.

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00:43:09,778 --> 00:43:13,596

[LAUGH] But it's the summary of the types of data we look at to assess the risk for

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00:43:13,596 --> 00:43:16,880

plant-incorporated protectants, thank you.

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00:43:16,880 --> 00:43:20,940

>> Dr. Barbero >> Okay, now we will hear from FDA about the types of data and

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00:43:20,940 --> 00:43:24,370

information that are important to them when they are making assessments.

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00:43:24,370 --> 00:43:25,010

>> Jason Dietz >> Thank you, Robbie.

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00:43:25,010 --> 00:43:29,410

And this particular slide refers to foods from genetically engineered plants.

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00:43:29,410 --> 00:43:33,000

When we talk about the genetically engineered animal in the case studies,

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00:43:33,000 --> 00:43:38,060

we'll have a similar slide that details those specific aspects.

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00:43:38,060 --> 00:43:42,190

I think it's important to understand that as a food producer, you have

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00:43:42,190 --> 00:43:46,650

an obligation to ensure that the foods that you produce are safe and lawful.

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00:43:46,650 --> 00:43:50,130

And to help firms ensure that they are meeting their legal obligation to

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00:43:50,130 --> 00:43:55,040

produce safe and lawful foods, FDA has established a consultation process

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00:43:55,040 --> 00:43:59,430

that allows firms to voluntarily engage with the agency prior to marketing

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00:43:59,430 --> 00:44:03,270

to make sure that their foods again, are safe and lawful.

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00:44:03,270 --> 00:44:07,791

Some of the information that we typically consider as you might expect,

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00:44:07,791 --> 00:44:11,421

we wanna know what the crop is, how it's typically used,

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00:44:11,421 --> 00:44:13,958

what it's intended change in the crop is?

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00:44:13,958 --> 00:44:19,121

And in terms of what you might think of as science based safety assessment

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00:44:19,121 --> 00:44:24,218

components, we wanna have a molecular characterization of the crop.

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00:44:24,218 --> 00:44:27,950

What has been inserted into it, what is expressed from it?

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00:44:27,950 --> 00:44:32,290

We wanna then also know, are the express materials, are they safe?

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00:44:32,290 --> 00:44:36,019

Are there any toxicity concerns, any allergenicity concerns?

638

00:44:37,240 --> 00:44:41,016

And we also wanna look at the levels of key nutrients, anti-nutrients, and

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00:44:41,016 --> 00:44:44,990

any endogenous toxicants that might be produced in the plant.

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00:44:44,990 --> 00:44:48,130

And I think another important point about this is this assessment

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00:44:48,130 --> 00:44:50,760

is performed on a case by case basis.

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00:44:50,760 --> 00:44:54,838

And this is very important because it gives us the flexibility to ensure that

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00:44:54,838 --> 00:44:59,140

the kinds of analyses performed are those most relevant to your crop.

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00:44:59,140 --> 00:45:02,899

For example, the kind of things that we might look at in corn may be very

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00:45:02,899 --> 00:45:04,318

different from a tomato.

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00:45:04,318 --> 00:45:08,692

And so, one of the unique features of this program is that you have the ability

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00:45:08,692 --> 00:45:10,998

to come to us very early in development,

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00:45:10,998 --> 00:45:16,222

long before you have produced a product, to engage with us and

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00:45:16,222 --> 00:45:18,870

talk us about your product.

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00:45:18,870 --> 00:45:21,680

And we can give you feedback in the kinds of safety and

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00:45:21,680 --> 00:45:23,900

legal issues that you should be considering.

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00:45:23,900 --> 00:45:25,600

And I think that as you walk through the case studies,

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00:45:25,600 --> 00:45:28,360

you'll hear that more than a few times.

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00:45:28,360 --> 00:45:33,360

So with that, I would leave you with the message here that remember,

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00:45:33,360 --> 00:45:36,290

your objective is to ultimately get to safety.

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00:45:36,290 --> 00:45:38,651

There may be many paths that can get you there.

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00:45:38,651 --> 00:45:44,150

But it is tremendously useful to come and talk to the agency prior to marketing,

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00:45:44,150 --> 00:45:49,400

and the earlier in development, the better.

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00:45:49,400 --> 00:45:50,260

>> Dr. Barbero >> Okay.

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00:45:50,260 --> 00:45:54,360

Thank you very much for those overviews.

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00:45:54,360 --> 00:45:58,700

At this point, what we will do is walk through two case studies

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00:45:58,700 --> 00:46:04,050

in the category we're calling products for human food and animal feed.

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00:46:04,050 --> 00:46:05,380

I will present the case study.

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00:46:05,380 --> 00:46:09,110

So, you have these case studies in the packets that you

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00:46:09,110 --> 00:46:10,120

received when you walked in.

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00:46:10,120 --> 00:46:14,980

If you're watching online, they're available on the DFS website.

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00:46:14,980 --> 00:46:21,000

They're also available in docket associated with these meetings.

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00:46:21,000 --> 00:46:23,610

What I will do is give you a very high level overview of them, and

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00:46:23,610 --> 00:46:25,900

then each of the agencies will walk through,

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00:46:27,370 --> 00:46:32,560

why they would have oversight responsibility, and what

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00:46:32,560 --> 00:46:35,290

the levels of engagement you would need to have with each of those agencies is.

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00:46:35,290 --> 00:46:39,020

We'll do both of these two case studies, in this category first.

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00:46:39,020 --> 00:46:43,002

And then I will start a timer and we'll take about 20 minutes of Q&A.

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00:46:43,002 --> 00:46:49,450

And then we run out of that time, we will stop and move on to the next category.

### Case Study: Hypothetical GE Corn with Pesticidal Properties

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00:46:49,450 --> 00:46:54,640

So, the first product here is case study number one in your packet.

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00:46:56,030 --> 00:47:00,720

It's a hypothetical genetically engineered corn with pesticidal properties.

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00:47:00,720 --> 00:47:04,780

It's a field crop used for food for humans and animals.

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00:47:04,780 --> 00:47:07,350

It's engineered with a plant pest component to have

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00:47:07,350 --> 00:47:10,670

pesticidal activity against certain insects.

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00:47:10,670 --> 00:47:13,800

The product corn, is *Zea mays* is

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00:47:13,800 --> 00:47:18,090

genetically engineered to express a protein with pesticidal activity.

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00:47:18,090 --> 00:47:22,359

The gene encoding the protein is isolated from the bacteria *Bacillus thuringiensis*.

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00:47:22,359 --> 00:47:26,849

And is controlled by the Cauliflower Mosaic Virus 35s Promoter.

684

00:47:26,849 --> 00:47:30,443

The construct is integrated into a binary vector and

685

00:47:30,443 --> 00:47:36,980

introduced into the corn genome using agrobacterium mediated transformation.

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00:47:36,980 --> 00:47:42,270

Also on that vector and stably incorporated into the corn genome,

687

00:47:42,270 --> 00:47:46,190

is a gene that enables selection of transformants during R&D.

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00:47:46,190 --> 00:47:48,221

So which agencies have oversight and why?

689

00:47:48,221 --> 00:47:52,851

Well the USDA has oversight because the genetically engineered corn

690

00:47:52,851 --> 00:47:55,817

is engineered with a plant pest component.

691

00:47:55,817 --> 00:48:01,180

The EPA has oversight, because the DNA codes for a pesticidal trait.

692

00:48:01,180 --> 00:48:05,471

And the FDA has oversight, because the genetically engineered corn will be used

693

00:48:05,471 --> 00:48:07,503

for food for humans and/or animals.

694

00:48:11,368 --> 00:48:15,850

>> Dr. Hoffman >> So, the USDA would be involved in regulating this corn product.

695

00:48:15,850 --> 00:48:22,250

As I mentioned before in the R&D phase, which is normally in a green house or

696

00:48:22,250 --> 00:48:26,808

a growth chambers, that the only authorization that would be required from

697

00:48:26,808 --> 00:48:32,770

APHIS would be an authorization for interstate movement or import.

698

00:48:32,770 --> 00:48:38,680

Then when the developer gets to the point where they do small or large field trials,

699

00:48:38,680 --> 00:48:44,350

authorization would, in addition, be needed for the environmental release.

700

00:48:44,350 --> 00:48:47,250

We have a NEPA obligation.

701

00:48:47,250 --> 00:48:53,410

Our NEPA implementing regulations have a categorically

702

00:48:53,410 --> 00:48:58,070

exclusion from NEPA for confined field trials.

703

00:48:58,070 --> 00:49:02,260

The reasoning is that confined field trials are confined,

704

00:49:02,260 --> 00:49:07,910

so the exposure of that organism in the environment is negligible.

705

00:49:07,910 --> 00:49:13,220

And that there is not a need to do NEPA.

706

00:49:13,220 --> 00:49:17,135

And I'll be describing some examples where

707

00:49:17,135 --> 00:49:21,810

we have exceptions to that categorical exclusion.

708

00:49:21,810 --> 00:49:28,450

At the commercialization stage, usually developers petition

709

00:49:28,450 --> 00:49:34,380

the APHIS for non-regulated status prior to commercialization.

710

00:49:34,380 --> 00:49:40,302

And at that time, we would, as I described before, do plant pest risk assessment and,

711

00:49:40,302 --> 00:49:45,906

in complying with NEPA, we would typically do either environmental assessment,

712

00:49:45,906 --> 00:49:48,480

or environmental impact statement.

713

00:49:52,695 --> 00:49:54,658

>> Unknown speaker >> You say unregulated status.

714

00:49:54,658 --> 00:49:58,470

Would you mind describing what that actually means?

715

00:49:58,470 --> 00:49:59,890

>> Dr. Hoffman >> Are we gonna take questions now?

716

00:49:59,890 --> 00:50:00,870

>> Dr. Barbero >> Yes, so can you hold that question?

717

00:50:00,870 --> 00:50:01,647

What we can do that.

718

00:50:01,647 --> 00:50:03,736

We can hit on that one but we'll.

719

00:50:03,736 --> 00:50:05,687

[CROSSTALK] Yeah.

720

00:50:05,687 --> 00:50:09,143

>> Unknown Speaker >> You keep saying regulated, unregulated-

>> Dr. Barbero >> Do you wanna briefly describe what you

721

00:50:09,143 --> 00:50:14,348

mean by-

>> Dr. Hoffman >> Okay, so if a GE organism triggers our

722

00:50:14,348 --> 00:50:19,878

regulation then it has regulated status.

723

00:50:19,878 --> 00:50:25,050

If at a certain time when information is collected about that

724

00:50:25,050 --> 00:50:33,050

organism a developer can petition the USDA for granting non-regulated status.

725

00:50:33,050 --> 00:50:37,742

And at that time, they submit a dossier

726

00:50:37,742 --> 00:50:42,570

to the agency that includes some information.

727

00:50:42,570 --> 00:50:49,260

I had an earlier slide which described the type of information that the company might

728

00:50:49,260 --> 00:50:54,430

submit to us, and we would do a comprehensive review of the information.

729

00:50:54,430 --> 00:50:58,738

They submit it and any other information in the literature that's relevant.

730

00:50:58,738 --> 00:51:02,940

And we would decide whether or not it poses a plant pest risk.

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00:51:02,940 --> 00:51:06,740

And if not, if it does not pose a plant pest risk, then we would

732

00:51:06,740 --> 00:51:11,450

grant a non-regulated status and permits would no longer be required for

733  
00:51:11,450 --> 00:51:15,843  
the importation, interstate movement, or environmental release of those organisms.

734  
00:51:15,843 --> 00:51:19,506  
>> Unknown Speaker >> So I don't get exactly.

735  
00:51:19,506 --> 00:51:22,361  
You say we collect information.

736  
00:51:22,361 --> 00:51:24,740  
Who are you collecting the information from?

737  
00:51:24,740 --> 00:51:27,517  
>> Dr. Hoffman >> The developer puts together a dossier.

738  
00:51:27,517 --> 00:51:33,150  
>> Unknown Speaker >> So, just whoever designed the thing-  
>> Dr. Hoffman >> The person

739  
00:51:33,150 --> 00:51:37,740  
who's making the petition, the petition-  
>> [INAUDIBLE]

740  
00:51:37,740 --> 00:51:39,540  
>> The petition is a collection of

741  
00:51:39,540 --> 00:51:40,325  
information.

742  
00:51:40,325 --> 00:51:41,720  
>> Dr. Hoffman >>Okay.

743  
00:51:41,720 --> 00:51:44,971  
>> Dr. Barbero >> We can take this one offline.

744  
00:51:44,971 --> 00:51:47,450  
I want to make sure we have a chance to get through all of these.

745  
00:51:47,450 --> 00:51:48,094  
Yeah.  
>> Unknown Speaker >> Okay,

746

00:51:48,094 --> 00:51:50,774

I'm just making sure I'm getting it because he keeps opening it up, so

747

00:51:50,774 --> 00:51:52,560

I'm just trying to make sure-

>> Dr. Barbero >> Yeah, so.

748

00:51:52,560 --> 00:51:57,271

>> Dr. Hoffman >> Why don't I talk with you offline

>> Unknown Speaker >> Okay we'll do the interview after

749

00:51:57,271 --> 00:51:58,863

the [CROSSTALK]

>> Dr. Hoffman >> Sure.

750

00:51:58,863 --> 00:52:00,316

>> Unknown Speaker >> Awesome.

751

00:52:00,316 --> 00:52:01,697

>> Dr. Barbero >> Okay.

752

00:52:01,697 --> 00:52:03,440

Neil, anything else on this, or are you?

753

00:52:03,440 --> 00:52:04,650

Okay.

754

00:52:04,650 --> 00:52:05,170

But this is good.

755

00:52:05,170 --> 00:52:06,260

I appreciate these questions.

756

00:52:06,260 --> 00:52:08,417

I mean I think that there is, as Mike indicated,

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00:52:08,417 --> 00:52:11,643

a lot of jargon that gets used here, and this is important information.

758

00:52:11,643 --> 00:52:12,503

>> Unknown Speaker >> Sure.

759

00:52:12,503 --> 00:52:16,852

Is that one of the major changes that we're doing with this

760

00:52:16,852 --> 00:52:21,270

meeting is it the deregulating

>> Dr. Barbero >> So, let's take this offline.

761

00:52:21,270 --> 00:52:22,133

I want to make sure that.

762

00:52:22,133 --> 00:52:22,714

Okay. All right. Thank you.

763

00:52:22,714 --> 00:52:24,538

Okay.

764

00:52:24,538 --> 00:52:25,676

Okay.

765

00:52:25,676 --> 00:52:26,918

Finished, Neil?

766

00:52:26,918 --> 00:52:27,430

>> Dr. Hoffman >> Mm-hm.

>> Dr. Barbero >> Okay.

767

00:52:27,430 --> 00:52:28,610

All right, Mike.

768

00:52:28,610 --> 00:52:32,470

>> Mike Mendelsohn >> Okay, I'd like to talk about what we look at with PIP, so again,

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00:52:32,470 --> 00:52:38,000

in the way EPA looks at in the pesticide program, is that it's a genetic material

770

00:52:38,000 --> 00:52:42,140

necessary for the production, and the pesticidal substance in the plant.

771

00:52:42,140 --> 00:52:43,560

So, it's small scale.

772

00:52:43,560 --> 00:52:45,740

Largely the EPA is not involved.

773

00:52:45,740 --> 00:52:48,770

It's under ten acres of testing.

774

00:52:49,860 --> 00:52:54,760

Larger than ten acres, EPA requires an experimental use permit.

775

00:52:54,760 --> 00:52:58,740

So, this is prior to the commercialization of the product.

776

00:52:58,740 --> 00:53:02,564

But at large scale testing, we require

777

00:53:02,564 --> 00:53:08,950

the petitioner to go ahead and to obtain an experimental use permit,

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00:53:08,950 --> 00:53:15,060

which is a permit that allows the field testing of the plant over ten acres.

779

00:53:16,385 --> 00:53:19,750

In addition to that, in addition to the experimental use permit,

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00:53:19,750 --> 00:53:23,300

EPA requires a temporary tolerance exemption.

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00:53:23,300 --> 00:53:29,840

So the one is for the use of the material in the field and

782

00:53:29,840 --> 00:53:34,170

the other one is for the residue of the pesticidal substance in the food.

783

00:53:34,170 --> 00:53:39,880

So we require a temporary tolerance exemption for that.

784

00:53:39,880 --> 00:53:46,224

When we get to commercialization, the EPA requires a permanent tolerance exemption,

785

00:53:46,224 --> 00:53:52,053

which is a regulation allowing the residue of that pesticide substance in food,

786

00:53:52,053 --> 00:53:54,041  
as well as a registration.

787

00:53:54,041 --> 00:53:58,860  
As to register the plant incorporated protectant.

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00:53:58,860 --> 00:54:01,625  
The registration is a license that allows the sale and

789

00:54:01,625 --> 00:54:03,352  
distribution of the pesticide.

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00:54:07,544 --> 00:54:10,260  
[NOISE]  
>> Jason Dietz >> Thank you.

791

00:54:10,260 --> 00:54:14,590  
And for the FDA perspective, this is a crop that's going to be used for food.

792

00:54:14,590 --> 00:54:18,750  
Presumably food for humans and animals, so certainly that food must meet

793

00:54:18,750 --> 00:54:22,080  
the standards in their Federal Food, Drug and Cosmetic Act.

794

00:54:23,310 --> 00:54:25,870  
Generally, for genetically engineered plants,

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00:54:25,870 --> 00:54:30,560  
we would strongly suggest that a developer complete a voluntary consultation  
with

796

00:54:30,560 --> 00:54:35,100  
the agency prior to marketing, and that traditionally has been the process

797

00:54:35,100 --> 00:54:37,830  
through which developers have entered the marketplace.

798

00:54:38,830 --> 00:54:43,150  
While developers may not necessarily come to us during the research and  
development

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00:54:43,150 --> 00:54:47,460

phase, as I mentioned earlier, the earlier you consult with us, generally the better.

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00:54:47,460 --> 00:54:50,402

The better for the agency, and the better for you,

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00:54:50,402 --> 00:54:53,926

It gives you a more predictable regulatory process and

802

00:54:53,926 --> 00:54:56,888

decisions that you make in your research and

803

00:54:56,888 --> 00:55:02,530

development phase may impact the regulatory aspects of your product.

804

00:55:02,530 --> 00:55:05,130

So certainly, as you move from research and

805

00:55:05,130 --> 00:55:09,458

development to small scale field trials and then to larger scale field trials,

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00:55:09,458 --> 00:55:13,430

it's useful to consult with us because we can help give you

807

00:55:13,430 --> 00:55:18,130

feedback that you can use to incorporate into the design of your field trials and

808

00:55:18,130 --> 00:55:21,710

the information that you might collect as part of your field trials.

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00:55:21,710 --> 00:55:26,340

And once you have completed your trial work, you can then submit a summary

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00:55:26,340 --> 00:55:28,490

of your safety and nutritional information to FDA.

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00:55:28,490 --> 00:55:32,250

We have a team of scientists there that would evaluate it.

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00:55:32,250 --> 00:55:36,450

Once we are satisfied that there are no outstanding food safety or legal issues,

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00:55:36,450 --> 00:55:40,464

we will respond to you with a letter indicating that we have no questions about

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00:55:40,464 --> 00:55:41,844

your safety assessment.

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00:55:41,844 --> 00:55:46,674

And then we will post on the Internet a memo that describes the consultation and

816

00:55:46,674 --> 00:55:49,463

a copy of the letter that has been sent to you.

817

00:55:49,463 --> 00:55:52,485

And I think, again as I mentioned earlier,

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00:55:52,485 --> 00:55:57,225

I think the key with this particular case study is the consultation,

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00:55:57,225 --> 00:56:02,470

well in advance of commercialization, and early in development.

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00:56:02,470 --> 00:56:05,910

Again, I can't say it enough but that makes it a predictable process for you,

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00:56:05,910 --> 00:56:08,170

and a predictable process for us.

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00:56:08,170 --> 00:56:12,160

And it also helps us identify issues very early, in the process.

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00:56:12,160 --> 00:56:12,660

Thank you.

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00:56:14,750 --> 00:56:18,140

>> Dr. Barbero >> Okay, so now we will do the second case study in this product category.

## Case Study: Hypothetical Herbicide-Tolerant Canola

825

00:56:18,140 --> 00:56:20,970

This is case study number three, in the packets that you have with you.

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00:56:22,080 --> 00:56:25,960

It is a hypothetical genetically engineered, herbicide tolerant canola.

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00:56:25,960 --> 00:56:30,530

It's a field crop used as food for humans, and, or animals, that is genetically

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00:56:30,530 --> 00:56:35,800

engineered with a plant pest component, to tolerate an already registered herbicide.

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00:56:35,800 --> 00:56:40,640

This particular herbicide has not previously been used on plants used for food for

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00:56:40,640 --> 00:56:41,740

animals.

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00:56:41,740 --> 00:56:45,150

The product is a domesticated canola, *Brassica napus*,

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00:56:45,150 --> 00:56:48,790

that is genetically engineered to tolerate an herbicide by increasing the expression

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00:56:48,790 --> 00:56:51,270

of a gene found in the canola genome,

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00:56:51,270 --> 00:56:56,260

using the constitutive 35S Cauliflower Mosaic Virus promoter.

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00:56:56,260 --> 00:57:00,440

Extracted canola oils will be used for bio diesel production, and

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00:57:00,440 --> 00:57:05,130

the remaining bio mass will be processed into meal for food for animals,

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00:57:06,130 --> 00:57:11,840

and the animal or products of the animal may subsequently be consumed by humans.

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00:57:11,840 --> 00:57:14,560

The 35S Cauliflower Mosaic Virus promoter and

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00:57:14,560 --> 00:57:18,560

the canola gene are co-introduced into the plant using a biolistic approach.

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00:57:18,560 --> 00:57:22,610

Because the canola gene confers resistance to an herbicide, no additional selectable

841

00:57:22,610 --> 00:57:24,040

marker is required.

842

00:57:24,040 --> 00:57:27,880

This particular herbicide, Herbicide X, is already registered by the EPA, but

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00:57:27,880 --> 00:57:30,879

is not yet approved for use on animal, food crops.

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00:57:31,940 --> 00:57:35,100

And in quotes they are new food use, that's a term right there.

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00:57:35,100 --> 00:57:38,040

In this scenario, a single developer produces both the herbicide

846

00:57:38,040 --> 00:57:40,440

resistant canola and the herbicide.

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00:57:40,440 --> 00:57:42,180

So which agencies have oversight and why?

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00:57:43,970 --> 00:57:46,550

The USDA has oversight because the herbicide tolerant plant

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00:57:46,550 --> 00:57:49,079

is genetically engineered with plant pest components.

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00:57:50,160 --> 00:57:55,270

The EPA has oversight because it regulates the new use of the herbicide itself,

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00:57:55,270 --> 00:57:57,470

not the genetic material used to engineer the plant.

852

00:57:57,470 --> 00:58:02,030

And the FDA has oversight because the GE canola will be used for food for

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00:58:02,030 --> 00:58:03,290

humans and or animals.

854

00:58:05,600 --> 00:58:08,950

>> Dr. Hoffman >> So the USDA would have pretty much the identical role for

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00:58:08,950 --> 00:58:11,300

this product as the last one that I described.

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00:58:11,300 --> 00:58:14,530

I'll just go very briefly, you would need authorization for

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00:58:14,530 --> 00:58:16,870

movement during the R&D phase.

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00:58:16,870 --> 00:58:19,990

You would need permits or notifications and authorization for

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00:58:19,990 --> 00:58:24,500

the environmental release during the small or large scale field testing.

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00:58:24,500 --> 00:58:27,210

This particular product, we would be very familiar with.

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00:58:27,210 --> 00:58:31,350

It would be categorically excluded from NEPA during field testing.

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00:58:31,350 --> 00:58:34,918

At the time of granting for a petition for

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00:58:34,918 --> 00:58:40,880

non-regulated status, then we would do plant-pest risk assessment,

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00:58:40,880 --> 00:58:45,370

and do a NEPA analysis would typically be an environmental assessment.

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00:58:51,400 --> 00:58:56,220

>> Mike Mendelsohn >> So, as Robbie said, for EPA, we're not regulating the PIP, this is not a PIP.

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00:58:56,220 --> 00:58:59,460

We're not regulating genetic material, we, simply in this case ,regulate

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00:58:59,460 --> 00:59:04,370

the chemical herbicide that's associated with the use of the plant.

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00:59:04,370 --> 00:59:09,620

So, in this particular case, prior to small scale field trials,

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00:59:10,740 --> 00:59:12,990

we don't have oversight.

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00:59:12,990 --> 00:59:17,170

At the large scale field trials, if the company were to do that,

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00:59:17,170 --> 00:59:21,650

they would need to get an experimental use permit and

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00:59:21,650 --> 00:59:26,030

a temporary tolerance exemption or temporary tolerance for the herbicide.

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00:59:26,030 --> 00:59:30,110

In practice, most companies test at a smaller scale.

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00:59:30,110 --> 00:59:33,720

We don't really see EUPs for these that often.

875

00:59:34,970 --> 00:59:37,530

Prior to commercialization of the herbicide,

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00:59:37,530 --> 00:59:42,940

this is commercializing the pesticide, the herbicide use for use on this crop.

877

00:59:42,940 --> 00:59:46,970

Why is this different than the current uses?

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00:59:46,970 --> 00:59:51,000

Many times, it's a different rate, a different timing of the application or

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00:59:51,000 --> 00:59:57,410

sometimes, a different crop, and for those, we would need to get a tolerance,

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00:59:57,410 --> 01:00:02,510

for the herbicide, to allow for the residues of the herbicide in the food.

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01:00:02,510 --> 01:00:07,200

And, we would amend the herbicide, pesticide product registration.

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01:00:07,200 --> 01:00:09,550

Or, another way that that's done is,

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01:00:09,550 --> 01:00:13,873

most companies would obtain a new registration, for that use.

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01:00:13,873 --> 01:00:17,009

So again, for EPA's side, we would look at,

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01:00:19,390 --> 01:00:23,750

getting a tolerance in place for the herbicide being used on that food crop.

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01:00:23,750 --> 01:00:28,330

And also having a registration in place or an amendment to an existing

887

01:00:28,330 --> 01:00:33,370

registration that would allow the use of that herbicide on that crop.

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01:00:38,100 --> 01:00:39,620

>> Jason Dietz >> From the FDA perspective again,

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01:00:39,620 --> 01:00:44,510

this is a crop that we use for food and so not much

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01:00:44,510 --> 01:00:48,550

will change from the situation with corn except that we're dealing with canola.

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01:00:48,550 --> 01:00:52,990

And that is relevant to our a case by case safety assessment because our

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01:00:52,990 --> 01:00:56,980

safety assessment will focus on the key aspects of canola, in this instance,

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01:00:56,980 --> 01:00:58,790

instead of corn.

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01:00:58,790 --> 01:01:00,380

And as I mentioned before,

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01:01:00,380 --> 01:01:05,010

it's always good to contact us early in development and as often as necessary,

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01:01:05,010 --> 01:01:10,080

and that helps produce a good product for you and a predictable regulatory process.

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01:01:13,340 --> 01:01:14,270

>> Dr. Barbero >> Okay.

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01:01:14,270 --> 01:01:16,980

So, we have now gone through these two case studies.

## Case Studies Q&A Period for Products for Human and Animal Feed

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01:01:16,980 --> 01:01:22,780

What I'd like to do here, is allow about 20 minutes for questions.

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01:01:22,780 --> 01:01:24,500

What I'd like you to do is just raise your hand.

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01:01:24,500 --> 01:01:26,700

We have some people with microphones.

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01:01:26,700 --> 01:01:30,640

So, you've already had a turn, let me do a circle around and get everybody else, and

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01:01:30,640 --> 01:01:31,800

then we can come back.

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01:01:32,970 --> 01:01:37,619

And basically, please say your name, and I think someone,

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01:01:37,619 --> 01:01:42,101

there's one here, yeah, and please make it a question.

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01:01:42,101 --> 01:01:45,130

If it seems to me like it's not a question,

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01:01:45,130 --> 01:01:50,274

I will just urge you to turn it into a question so that we can respond then.

908

01:01:50,274 --> 01:01:52,450

>> Okay, my name is Belinda Martineau, and

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01:01:52,450 --> 01:01:56,790

my questions apply to both of the case studies we've just gone over.

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01:01:56,790 --> 01:01:59,160

They have to do with oversight.

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01:01:59,160 --> 01:02:04,920

So, you say that USDA comes into it because of plant pest components,

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01:02:04,920 --> 01:02:09,040

but I thought that in other literature you've given out,

913

01:02:09,040 --> 01:02:14,100

you talk about whether it poses a plant pest risks.

914

01:02:14,100 --> 01:02:20,086

So, component of a plant pest don't necessarily pose a plant risk.

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01:02:20,086 --> 01:02:28,620

Then there are other GMOs that don't contain these plant pest components and

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01:02:28,620 --> 01:02:34,220

wouldn't come under their regulatory oversight and then with the FDA,

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01:02:34,220 --> 01:02:38,160

of course, it's not really->> Dr. Barbero >> So the question for USDA is.

918

01:02:38,160 --> 01:02:45,230

>> Belinda Martineau >> The question is, doesn't the product have to pose a plant

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01:02:45,230 --> 01:02:50,700

pest risk as opposed to just containing plant pest components?

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01:02:50,700 --> 01:02:52,100

>> Dr. Barbero >> Okay.

921

01:02:52,100 --> 01:02:58,520

>> Belinda Martineau >> For USDA, and then for FDA, the oversight, obviously, a company could,

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01:02:58,520 --> 01:03:03,490

since it's voluntary, not even show up for a consultation.

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01:03:03,490 --> 01:03:09,290

And couldn't the FDA use it's food additive authority to regulate

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01:03:09,290 --> 01:03:15,880

a foreign protein added to a genetically engineered plant as a food additive?

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01:03:15,880 --> 01:03:17,800

Which was what it did for

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01:03:17,800 --> 01:03:22,360

the first genetically engineered whole food that came through the FDA.

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01:03:22,360 --> 01:03:23,180

>> Dr. Barbero >> Okay, thank you.

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01:03:23,180 --> 01:03:24,410

Let's start with the USDA.

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01:03:24,410 --> 01:03:26,110

Is the question clear to you, Neil?

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01:03:26,110 --> 01:03:26,610

>> Dr. Hoffman >> Yes.

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01:03:27,650 --> 01:03:33,220

If a, a plant contains a plant pest component, it triggers our regulation.

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01:03:33,220 --> 01:03:37,739

And then it needs a permit, needs some authorization in order for

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01:03:37,739 --> 01:03:43,918

those three areas, importation, interstate movement, and environmental release.

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01:03:43,918 --> 01:03:50,019

If it doesn't pose a plant pest risk, that plant pest risk is evaluated

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01:03:50,019 --> 01:03:55,624

at the time of a petition for granting non-regulated status.

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01:03:55,624 --> 01:03:57,940

So, it is under regulation.

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01:03:57,940 --> 01:04:02,170

It's requiring a permit, because it has those plant pest components.

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01:04:02,170 --> 01:04:05,180

If we determine it doesn't pose a plant pest risk,

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01:04:05,180 --> 01:04:09,665

then we will grant non regulated status, and it no longer needs the permit.

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01:04:09,665 --> 01:04:12,820

I don't know if that answered your question.

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01:04:12,820 --> 01:04:17,622

>> Dr. Barbero >> So you're saying that if there's a plant pest component that there is,

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01:04:17,622 --> 01:04:22,598

you feel that it's important at that point to assess for a plant pest risk.

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01:04:22,598 --> 01:04:24,060

And that's why you do that?

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01:04:24,060 --> 01:04:28,997

>> Dr. Hoffman >> Yes, we don't actually assess whether it poses a plant pest risk

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01:04:28,997 --> 01:04:31,520

at the beginning of the process.

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01:04:32,720 --> 01:04:37,540

And, so if your question was whether or not.

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01:04:40,410 --> 01:04:43,560

Actually I'm not absolutely certain about your question.

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01:04:43,560 --> 01:04:45,385

You were making it, you were right.

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01:04:45,385 --> 01:04:48,430

There's a distinction between a plant pest component whether it

950

01:04:48,430 --> 01:04:50,180

poses a plant pest risk.

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01:04:50,180 --> 01:04:54,952

If we determine it doesn't pose a plant pest risk at the time of a petition for

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01:04:54,952 --> 01:04:59,521

granting non-regulated status, we will not continue to regulate it.

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01:04:59,521 --> 01:05:02,397

>> Dr. Barbero >> Okay, Jason?

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01:05:02,397 --> 01:05:06,888

>> Jason Dietz >> Thank you, first I think it's important that we recognize that all food must be

955

01:05:06,888 --> 01:05:11,311

safe regardless of how it's produced whether it's produced through genetic

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01:05:11,311 --> 01:05:15,821

engineering or some other process the applicable provisions of the law apply.

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01:05:15,821 --> 01:05:19,671

One of the things that we do consider during the consultation process is whether

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01:05:19,671 --> 01:05:23,821

the new protein is in fact a food additive that would require food additive approval.

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01:05:23,821 --> 01:05:27,158

And if in fact we found that that particular protein or

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01:05:27,158 --> 01:05:31,980

any other added substance would have to go through the food additive approval

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01:05:31,980 --> 01:05:34,962

process before it could be lawfully marketed.

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01:05:34,962 --> 01:05:39,885

And you are correct that, in fact, the kanamycin resistance protein in

963

01:05:39,885 --> 01:05:44,727

the Flavr Savr tomato was one case where a protein added to a genetically

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01:05:44,727 --> 01:05:49,437

engineered plant was regulated through the food additive process.

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01:05:49,437 --> 01:05:52,864

>> Dr. Barbero >> Okay, next question.

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01:05:57,380 --> 01:05:58,123

You want to have one.

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01:05:58,123 --> 01:06:00,283

>> Unknown Speaker >>[INAUDIBLE]

>> Dr. Barbero >> Sure, you can have one more, yep.

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01:06:00,283 --> 01:06:06,357

>> Okay, so you're with the White House, right?

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01:06:06,357 --> 01:06:07,414

>> Dr. Barbero >> I work in the White House, yes.

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01:06:07,414 --> 01:06:07,994

>> Unknown Speaker >> Okay, right.

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01:06:07,994 --> 01:06:12,024

So are you familiar with Obama recently did,

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01:06:12,024 --> 01:06:18,510

maybe two years ago, a behavioral science Executive Order.

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01:06:18,510 --> 01:06:21,410

And if you are familiar with it, can you share with me,

974

01:06:21,410 --> 01:06:26,532

without me doing an ROI, what and

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01:06:26,532 --> 01:06:32,530

what manner is he using that Executive Order in this process.

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01:06:32,530 --> 01:06:35,370

>> Dr. Barbero >> So these questions are intended to be about the case studies

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01:06:35,370 --> 01:06:38,820

that we have here in front of us so that we can stick on the time here.

978

01:06:38,820 --> 01:06:39,440

>> Unknown Speaker >> My bad, I'm sorry.

979

01:06:39,440 --> 01:06:40,920

>> Dr. Barbero >> Yeah, no problem, that's all right.

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01:06:40,920 --> 01:06:43,830

Why don't we find each other- >> Unknown Speaker >> Is that something you can help

981

01:06:43,830 --> 01:06:45,650

me with later?

982

01:06:45,650 --> 01:06:47,690

>> Dr. Barbero >> If we have time, let's find a chance to connect offline.

983

01:06:47,690 --> 01:06:48,410

>> Unknown Speaker >> Okay.

>> Dr. Barbero >> Thank you.

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01:06:50,910 --> 01:06:51,410

Over here.

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01:06:53,610 --> 01:06:58,080

>> Unknown Speaker >> Unless I'm mistaken, do any of these case studies involve

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01:06:58,080 --> 01:07:02,010

cisgenic processes or any of the new gene drive processes?

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01:07:02,010 --> 01:07:06,931

It seems like they all contain some kind of transgene component.

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01:07:06,931 --> 01:07:08,625

Is that true?

989

01:07:08,625 --> 01:07:14,627

And if they, where do the cisgenic and the gene drive and

990

01:07:14,627 --> 01:07:21,154

gene editing procedures come under regulatory framework.

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01:07:21,154 --> 01:07:21,999

>> Dr. Barbero >> So yeah, so

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01:07:21,999 --> 01:07:27,830

these case studies are in the discussion here is just limited to what's in these.

993

01:07:27,830 --> 01:07:31,458

To the extent that you have questions about other related issues,

994

01:07:31,458 --> 01:07:34,262

let's find a time to connect and talk about those.

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01:07:34,262 --> 01:07:37,388

>> Unknown Speaker >> I thought that they were related because I'm asking about the case studies.

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01:07:37,388 --> 01:07:41,485

And have case studies, where do they fall?

997

01:07:41,485 --> 01:07:47,568

Are any of these, are any of these cisgenic processes?

998

01:07:47,568 --> 01:07:49,671

Are any of them gene drive processes?

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01:07:49,671 --> 01:07:51,469

Or are they all transgenes?

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01:07:51,469 --> 01:07:53,036

That's the question.

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01:07:53,036 --> 01:07:55,478

>> Dr. Barbero >> There are no gene drives in these case studies.

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01:07:55,478 --> 01:07:57,290

Are there cisgenic?

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01:07:57,290 --> 01:07:59,560

I don't believe that there are.

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01:08:00,620 --> 01:08:05,580

>> Unknown Speaker >> And why was it chosen to not include the new technologies in any of the case

1005

01:08:05,580 --> 01:08:06,323

studies?

1006

01:08:06,323 --> 01:08:11,910

>> Dr. Barbero >> So that these case studies were derived in order to give

1007

01:08:11,910 --> 01:08:18,022

an overview of how the current products-

>> Unknown Speaker >> That are being developed or

1008

01:08:18,022 --> 01:08:19,639

that are on the market?

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01:08:19,639 --> 01:08:24,201

>> Dr. Barbero >> To the best extent possible to give an overview of the current roles and

1010

01:08:24,201 --> 01:08:28,410

responsibilities for current products of biotechnology.

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01:08:28,410 --> 01:08:32,576

>> Unknown Speaker >> So can I assume maybe that there is no regulatory framework for

1012

01:08:32,576 --> 01:08:36,833

the cisgenes and the gene drive and SIM biotechnologies then?

1013

01:08:36,833 --> 01:08:39,828

>> Dr. Barbero >> I don't think that that's a safe assumption to make.

1014

01:08:39,828 --> 01:08:41,894

Why don't we find a time to connect offline.

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01:08:41,894 --> 01:08:43,683

There will be a lot of opportunity for

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01:08:43,683 --> 01:08:46,062

this discussion during the breakout sessions.

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01:08:46,062 --> 01:08:48,875

>> Unknown Speaker >> Actually, I'd like it to be either in a breakout session or

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01:08:48,875 --> 01:08:50,465

something that isn't offline.

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01:08:50,465 --> 01:08:51,717

>> Dr. Barbero >> So, during the breakout sessions.

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01:08:51,717 --> 01:08:52,343

>> Unknown Speaker >> Thanks.

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01:08:52,343 --> 01:08:57,115

>> Dr. Barbero >> I would encourage you to bring this topic up and discuss it then, okay?

1022  
01:08:57,115 --> 01:08:58,694  
Thank you.

1023  
01:08:58,694 --> 01:09:04,690  
>> [INAUDIBLE].

1024  
01:09:04,690 --> 01:09:05,950  
>> Dr. Barbero >> Can you? Let's use the microphone, so

1025  
01:09:05,950 --> 01:09:07,770  
that we can get this transcribed.

1026  
01:09:07,770 --> 01:09:08,810  
And, can we get your name as well?

1027  
01:09:08,810 --> 01:09:11,934  
>> Yeah, I'm Josh Wilson, hi, people.

1028  
01:09:14,240 --> 01:09:17,105  
This is the first time I've ever engaged with any stakeholders.

1029  
01:09:17,105 --> 01:09:18,950  
Cuz all I do is write you guys letters.

1030  
01:09:18,950 --> 01:09:22,840  
And I never hear anything back so, it's a big black hole all my words.

1031  
01:09:22,840 --> 01:09:25,220  
So, this is kinda cool, it's interactive.

1032  
01:09:25,220 --> 01:09:29,150  
Okay, so let's be hypothetical here, we take this product, and

1033  
01:09:29,150 --> 01:09:31,460  
we deregulated APHIS.

1034  
01:09:31,460 --> 01:09:35,970  
So now it's deregulated so we can do whatever we want, it's open.

1035  
01:09:35,970 --> 01:09:39,410  
We have no records, we don't need to ask the company to

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01:09:39,410 --> 01:09:42,550

tell us how many hectares are going, or anything like that.

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01:09:42,550 --> 01:09:48,230

It doesn't matter it's completely free to do whatever it does.

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01:09:48,230 --> 01:09:50,720

>> Dr. Barbero >> Which of these case studies are you talking about?

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01:09:50,720 --> 01:09:52,659

>> Josh Wilson >> It's deregulated, we have this product.

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01:09:52,659 --> 01:09:57,608

And now a seed seller wants to sell it to our public lands our public land managers,

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01:09:57,608 --> 01:09:59,197

and it's deregulating.

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01:09:59,197 --> 01:10:00,809

>> Dr. Barbero >> So, which product are you talking about?

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01:10:00,809 --> 01:10:05,115

>> Josh Wilson >> The hypothetical nonfood product.

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01:10:05,115 --> 01:10:07,101

>> Dr. Barbero >> But which of the two that we just went through?

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01:10:07,101 --> 01:10:10,108

So we talked about, do you have the booklet in front of you?

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01:10:10,108 --> 01:10:11,408

>> Josh Wilson >> The Canola would be fine.

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01:10:11,408 --> 01:10:14,147

>> Dr. Barbero >> Okay, so the genetically engineered canola.

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01:10:14,147 --> 01:10:15,470

That is herbicide tolerant.

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01:10:15,470 --> 01:10:16,063

>> Josh Wilson >> Right.

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01:10:16,063 --> 01:10:16,644

>> Dr. Barbero >> Okay.

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01:10:16,644 --> 01:10:20,973

>> Josh Wilson >> So this thing, we found that this works great with our ARS programs

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01:10:20,973 --> 01:10:24,854

in our public lands and BLM is finding a place for it, okay.

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01:10:24,854 --> 01:10:28,716

So would BLM would the land manager,

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01:10:28,716 --> 01:10:34,830

because it's deregulated, not have to be aware of that.

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01:10:34,830 --> 01:10:36,630

So, if the land manager is saying, well,

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01:10:36,630 --> 01:10:39,630

I think this canola thing, I just see what it does.

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01:10:39,630 --> 01:10:45,340

And they tell me it does everything great, would there be any,

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01:10:45,340 --> 01:10:50,510

because now that it's deregulated, would that bypass NEPA's Act for

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01:10:50,510 --> 01:10:55,550

the Bureau of Land Management to start applying the seed?

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01:10:55,550 --> 01:10:56,520

>> Dr. Hoffman >> At one time

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01:10:58,180 --> 01:11:03,680

genetically modified crops that were deregulated were planted on park land.

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01:11:03,680 --> 01:11:09,130

The Department of Interior has changed their policy, and to my understanding they

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01:11:09,130 --> 01:11:14,480

are no longer using GE crops on park land.

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01:11:14,480 --> 01:11:17,249

As far as Bureau of Land Management, I don't,

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01:11:17,249 --> 01:11:21,281

I imagine it's part of the Department of Interior and that would be-

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01:11:21,281 --> 01:11:22,929

>> Josh Wilson >> It is under DOI, correct.

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01:11:22,929 --> 01:11:28,769

>> Dr. Hoffman >> Yeah, so I'm not that familiar with the entire legal-

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01:11:28,769 --> 01:11:30,232

>> Josh Wilson >> I can fill you in after.

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01:11:30,232 --> 01:11:32,379

>> Dr. Hoffman >> Implications of that policy.

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01:11:32,379 --> 01:11:37,190

So I think the answer is no that they would not be using that.

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01:11:37,190 --> 01:11:41,983

There are some cases for example in Colorado, there was some public space and

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01:11:41,983 --> 01:11:46,272

there was interest in using that public space to grow GE sugar beets.

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01:11:46,272 --> 01:11:49,323

And then there was opposition to that and

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01:11:49,323 --> 01:11:53,010

I don't believe that they are using that space.

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01:11:53,010 --> 01:11:58,762

So, in some cases, there have been public input about whether or

1076  
01:11:58,762 --> 01:12:02,580  
not to use GE organisms on public space.

1077  
01:12:02,580 --> 01:12:05,380  
And there's been some

1078  
01:12:05,380 --> 01:12:09,890  
response to that public input when there has been an opposition to it.

1079  
01:12:09,890 --> 01:12:12,690  
>> Dr. Barbero >> And so Neil to the extent that someone from one of these agencies came to APHIS

1080  
01:12:12,690 --> 01:12:18,660  
to ask about the status of a product, what would APHIS' role in that be?

1081  
01:12:18,660 --> 01:12:21,338  
>> Dr. Hoffman >> Well, we would just say  
>> Josh Wilson >> [CROSSTALK] regulated.

1082  
01:12:21,338 --> 01:12:26,500  
>> Dr. Hoffman >> If we have deregulated it, we no longer have jurisdiction over it.

1083  
01:12:26,500 --> 01:12:31,760  
>> Josh Wilson >> But it is still patent, does it have to be patented to be deregulated?

1084  
01:12:31,760 --> 01:12:37,680  
I guess if somebody-  
>> Dr. Hoffman >> That's a different story.

1085  
01:12:37,680 --> 01:12:39,000  
It doesn't have to be.

1086  
01:12:39,000 --> 01:12:43,750  
We've already been doing this long enough that there is some

1087  
01:12:43,750 --> 01:12:47,370  
crops that have already come off patent.

1088  
01:12:47,370 --> 01:12:50,094  
So it doesn't have to be patented, no.

1089  
01:12:50,094 --> 01:12:55,170  
>> Dr. Barbero >> All right great so Josh let's move to the next set case of studies thank you.

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01:12:55,170 --> 01:12:58,340  
All right so with our next set of case studies and

1091  
01:12:58,340 --> 01:13:01,730  
actually we're going to do one under the products of biomedical engineering.

### Case Study: Hypothetical GE Rabbit

1092  
01:13:01,730 --> 01:13:04,160  
This is the hypothetical GE rabbit.

1093  
01:13:04,160 --> 01:13:12,050  
It is case study number eight, in your packet.

1094  
01:13:14,430 --> 01:13:18,990  
This is an animal that is genetically engineered to make a therapeutic protein,

1095  
01:13:18,990 --> 01:13:23,890  
recombinant insulin, for treatment of humans lacking this protein activity.

1096  
01:13:23,890 --> 01:13:31,500  
The product, the rabbit, *Oryctolagus cuniculus* genome is genetically engineered

1097  
01:13:31,500 --> 01:13:36,710  
to express recombinant human insulin for use downstream as a therapeutic protein

1098  
01:13:36,710 --> 01:13:40,460  
in the treatment of human patients lacking adequate functional insulin.

1099  
01:13:40,460 --> 01:13:44,540  
The human insulin coding sequence is controlled by a five prime bovine alpha

1100  
01:13:44,540 --> 01:13:48,830  
S1 casein promoter sequence to allow expression of recombinant insulin

1101  
01:13:48,830 --> 01:13:51,060  
protein in rabbit milk.

1102  
01:13:51,060 --> 01:13:53,670  
The construct is micro-injected into fertilized oocytes, and

1103  
01:13:53,670 --> 01:13:58,030  
the issuing embryos are transferred to the oviduct of a recipient.

1104  
01:13:58,030 --> 01:14:01,580  
Also encoded in the vector and stably incorporated into the rabbit genome

1105  
01:14:01,580 --> 01:14:05,710  
are upstream and downstream regulatory sequences that enable expression of

1106  
01:14:05,710 --> 01:14:11,160  
the included codon optimized human insulin coding sequence and insulator  
sequences

1107  
01:14:11,160 --> 01:14:14,110  
to minimize position effects at the locus of genome integration.

1108  
01:14:14,110 --> 01:14:18,120  
Once a germ line transgenic animal is identified as a founder animal it is

1109  
01:14:18,120 --> 01:14:22,380  
bred to establish a lineage of GE rabbits used in insulin expression in milk.

1110  
01:14:22,380 --> 01:14:24,040  
Which agencies have oversight and why?

1111  
01:14:25,080 --> 01:14:28,470  
The FDA has oversight because the recombinant DNA construct encoding

1112  
01:14:28,470 --> 01:14:31,500  
the recombinant human insulin coding sequence

1113  
01:14:31,500 --> 01:14:34,301  
is integrated into the genome of the GE rabbit.

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01:14:34,301 --> 01:14:39,150

It is regulated as a new animal drug by the FDA Center for Veterinary Medicine and

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01:14:39,150 --> 01:14:45,560

the recombinant insulin purified from the GE Rabbit milk

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01:14:45,560 --> 01:14:50,102

is regulated as a human drug by the FDA Center for Drug and Evaluation Research.

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01:14:50,102 --> 01:14:55,380

So, it's important to note that there are two components of FDA

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01:14:55,380 --> 01:14:58,810

that work together in providing oversight for this product.

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01:14:58,810 --> 01:15:00,290

With that, I will hand it over to Jason.

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01:15:00,290 --> 01:15:01,300

>> Jason Dietz >> Thank you Robbie.

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01:15:01,300 --> 01:15:01,940

As Robbie said,

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01:15:01,940 --> 01:15:05,910

this is an interesting case study because you have two FDA regulated products,

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01:15:05,910 --> 01:15:11,740

a new animal drug associated with the recombinant DNA construct in the rabbit

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01:15:11,740 --> 01:15:16,310

and the recombinant human insulin which would be a new drug for humans.

1125

01:15:16,310 --> 01:15:20,460

And there is a mechanism at the agency for Centers to interact with each other for

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01:15:20,460 --> 01:15:22,720

products just like this one.

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01:15:23,910 --> 01:15:28,261

So first, once you have identified the founder animal and

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01:15:28,261 --> 01:15:34,450

the lineage of animal that you want to evaluate for potential production,

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01:15:34,450 --> 01:15:39,190

you would come to the agency and request that an investigational new animal

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01:15:39,190 --> 01:15:43,590

drug file be opened and you would do that at the Center for Veterinary  
Medicine.

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01:15:43,590 --> 01:15:47,610

They're the folks who regulate all new animal drugs.

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01:15:47,610 --> 01:15:52,360

And this investigation on new animal drug file or INAD.

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01:15:52,360 --> 01:15:58,220

This would allow you to submit information to the agency as you collect it for

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01:15:58,220 --> 01:16:00,520

investigational purposes only.

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01:16:00,520 --> 01:16:02,770

Because again you're still in the development phase here.

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01:16:04,070 --> 01:16:07,285

And then prior to clinical trials with the insulin,

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01:16:07,285 --> 01:16:11,668

you would need to go to the Center for Drug Evaluation and Research, and

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01:16:11,668 --> 01:16:15,029

file an investigational new drug application there,

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01:16:15,029 --> 01:16:19,980

so that you could then begin your clinical trials using the insulin.

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01:16:19,980 --> 01:16:22,540

And then prior to commercialization,

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01:16:22,540 --> 01:16:26,940

you would need to submit a new animal drug application to the Center for

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01:16:26,940 --> 01:16:32,260

Veterinary Medicine, for the recombinant construct in the rabbit.

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01:16:32,260 --> 01:16:35,230

So that would be your new animal drug application.

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01:16:35,230 --> 01:16:41,200

Then you would also need to submit a new drug application to the Center for

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01:16:41,200 --> 01:16:45,116

Drug Evaluation and Research for the recombinant human insulin.

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01:16:45,116 --> 01:16:51,340

And then, both CVM would have to approve the new animal drug application

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01:16:51,340 --> 01:16:55,220

and CDER would have to approve the new drug application for

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01:16:55,220 --> 01:16:59,160

your product to be fully authorized.

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01:16:59,160 --> 01:17:02,110

And the standard that we would use is the standard that we use for

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01:17:02,110 --> 01:17:06,940

all new animal drugs and drugs in general, which is that it must be safe and

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01:17:06,940 --> 01:17:09,600

effective for its intended use.

1152

01:17:09,600 --> 01:17:11,301

If you wanna go to the next slide.

1153

01:17:14,808 --> 01:17:19,722

So we talked a little bit earlier today about some of the data requirements and

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01:17:19,722 --> 01:17:24,786

so this slide is intended to describe to you some of the kinds of information that

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01:17:24,786 --> 01:17:30,420

would be included as part of an INAD, investigational new animal drug file.

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01:17:30,420 --> 01:17:35,620

In that particular case, you would include information about the species under study,

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01:17:35,620 --> 01:17:39,060

the genes that you've introduced, what you would expect to be expressed,

1158

01:17:40,340 --> 01:17:43,890

in general the phenotype that you are expecting.

1159

01:17:43,890 --> 01:17:47,760

The INAD regulations do have some specificity to them in limiting

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01:17:47,760 --> 01:17:52,480

what you can do, and you must keep the animals under containment at this phase.

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01:17:52,480 --> 01:17:55,130

There is special labeling that would be associated with them,

1162

01:17:55,130 --> 01:17:58,300

because they are investigational new animal drugs.

1163

01:17:58,300 --> 01:18:01,189

There would also be special record keeping requirements.

1164

01:18:02,450 --> 01:18:06,470

You'd also have to ensure the proper disposition of the animals.

1165

01:18:06,470 --> 01:18:09,160

And you'd also have to notify the agency when you intend to

1166

01:18:09,160 --> 01:18:12,840

move generative material from one location to another.

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01:18:12,840 --> 01:18:15,710

And then some environmental considerations to consider

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01:18:15,710 --> 01:18:18,690

with the National Environmental Policy Act or NEPA.

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01:18:18,690 --> 01:18:23,160

And many of them may help to be satisfied by the fact that these animals would be

1170

01:18:23,160 --> 01:18:24,020

well contained,

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01:18:24,020 --> 01:18:25,550

would not be entering the food or

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01:18:25,550 --> 01:18:30,020

feed supply without some degree of authorization from CVM.

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01:18:30,020 --> 01:18:35,690

In fact, to date, the agency has approved two animals that produce pharmaceutical

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01:18:35,690 --> 01:18:40,730

substances, and neither of them are authorized to enter the food supply,

1175

01:18:40,730 --> 01:18:43,410

and they are highly contained.

1176

01:18:45,220 --> 01:18:48,590

So then to the new animal drug application,

1177

01:18:48,590 --> 01:18:50,800

some of the information that you would consider there.

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01:18:50,800 --> 01:18:53,730

Much of this is probably as you would expect.

1179

01:18:53,730 --> 01:18:56,460

We want a product identification,

1180  
01:18:56,460 --> 01:18:59,430  
molecular characterization of the DNA you intended to insert,

1181  
01:18:59,430 --> 01:19:03,420  
and then a characterization of what you actually did insert.

1182  
01:19:03,420 --> 01:19:07,060  
Phenotypic and genotypic characterization of the animal.

1183  
01:19:07,060 --> 01:19:11,410  
We'd also wanna know about the phenotypic and genotypic stability of the animal  
and

1184  
01:19:11,410 --> 01:19:14,990  
a plan that you have to ensure the phenotypic and

1185  
01:19:14,990 --> 01:19:17,000  
genotypic stability over time.

1186  
01:19:17,000 --> 01:19:20,320  
There would be food and feed safety assessment if

1187  
01:19:20,320 --> 01:19:24,200  
the animal were intended to be used for food or feed, in this case.

1188  
01:19:24,200 --> 01:19:27,980  
Where we've had biopharm animals to date, they have not been intended to be  
used for

1189  
01:19:27,980 --> 01:19:28,668  
food or feed.

1190  
01:19:28,668 --> 01:19:32,610  
And then you would also need an environmental safety assessment.

1191  
01:19:32,610 --> 01:19:35,569  
That could include information such as your containment,

1192  
01:19:35,569 --> 01:19:37,232  
the disposition of the animals.

1193  
01:19:37,232 --> 01:19:42,419  
And that is a good example of a case where it's very useful to consult

1194  
01:19:42,419 --> 01:19:47,515  
with the agency ahead of time so that you can receive their input and

1195  
01:19:47,515 --> 01:19:52,266  
expertise in how to prepare your environmental assessment.

1196  
01:19:52,266 --> 01:19:55,603  
And then you'd also need an effectiveness in claim validation.

1197  
01:19:55,603 --> 01:20:00,249  
That is, does the new animal drug do what you say it does?

1198  
01:20:00,249 --> 01:20:02,669  
And I would point out that we have a very good guidance on this.

1199  
01:20:02,669 --> 01:20:08,536  
Guidance 187 lays out a number of these factors and if you've not read it already,

1200  
01:20:08,536 --> 01:20:13,194  
I would suggest that you take a look at it if you have more questions.

1201  
01:20:13,194 --> 01:20:17,176  
Thank you.

## Case Study Q&A Hypothetical GE Rabbit

1202  
01:20:17,176 --> 01:20:20,178  
>> Dr. Barbero >> Okay, so we'll do about ten minutes of questions here.

1203  
01:20:20,178 --> 01:20:23,205  
I see someone standing up here in the middle, and just for

1204  
01:20:23,205 --> 01:20:27,196  
these various agencies, specific documents that we're talking about.

1205  
01:20:27,196 --> 01:20:31,536  
For example, if you wanna define guidance 187,

1206

01:20:31,536 --> 01:20:37,268

you could do a Google search for GFI or guidance for industry 187.

1207

01:20:37,268 --> 01:20:38,028

>> Hi, thank you.

1208

01:20:38,028 --> 01:20:39,608

My name is Dana Pearls.

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01:20:39,608 --> 01:20:45,680

This is a great case study, especially given the approval of the GE salmon.

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01:20:45,680 --> 01:20:49,970

So this example is a very clear example of something intended for

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01:20:49,970 --> 01:20:52,850

therapeutic treatment for humans.

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01:20:52,850 --> 01:20:58,092

However as we've just seen with GE salmon this was the process that

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01:20:58,092 --> 01:21:03,615

it went through as a new animal drug despite the fact that there aren't

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01:21:03,615 --> 01:21:08,953

medicinal therapeutic purposes for humans, and so nor was there a formal

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01:21:08,953 --> 01:21:15,818

environmental impact statement conducted despite a lot of controversial findings.

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01:21:15,818 --> 01:21:19,801

So I'm curious given the fact that GE Salmon and

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01:21:19,801 --> 01:21:23,978

a number of other animals that are in the pipeline for

1218

01:21:23,978 --> 01:21:28,658

approval don't serve therapeutic drug like purposes.

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01:21:28,658 --> 01:21:33,298

Is this the same process moving forward intended for

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01:21:33,298 --> 01:21:38,368

GE animals and I don't know if GE insects would be there?

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01:21:38,368 --> 01:21:43,558

How will these animals, moving forward, be regulated?

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01:21:43,558 --> 01:21:48,171

And is it possible that there would be an independent committee as there has

1223

01:21:48,171 --> 01:21:49,278

been in the past?

1224

01:21:49,278 --> 01:21:51,198

Would that be resurrected?

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01:21:51,198 --> 01:21:54,612

And also, just to tag on that, a lot of these new GE animals

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01:21:54,612 --> 01:21:58,756

being researched are using new gene editing techniques like CRISPR.

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01:21:58,756 --> 01:22:02,528

>> Dr. Barbero >> So, Dana, I'm going to ask you to focus the question just on this case study,

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01:22:02,528 --> 01:22:04,138

to the extent that's possible.

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01:22:04,138 --> 01:22:06,930

When you want to discuss some of these other issues,

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01:22:06,930 --> 01:22:09,728

I think we should do those in the breakout sessions.

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01:22:09,728 --> 01:22:15,070

>> Dana Perls >> So I'd like for everybody to be able to hear, cuz this is a super specific example

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01:22:15,070 --> 01:22:20,510

that doesn't seem to apply to a lot of the GE animals coming through the pipeline.

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01:22:20,510 --> 01:22:25,747

So for those is this the process that it will be ushered into or

1234

01:22:25,747 --> 01:22:32,438

is there a more robust process for things that aren't for human treatments?

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01:22:32,438 --> 01:22:36,298

>> Dr. Barbero >> So I think these questions are best done if you can focus on a specific.

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01:22:36,298 --> 01:22:39,060

Do you have a specific case that you would like to-

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01:22:39,060 --> 01:22:41,566

>> Dana Perls >> For example, Aqua Bounty has suggested

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01:22:41,566 --> 01:22:46,354

that they will be putting another GE fish, GE rainbow trout, on the market or

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01:22:46,354 --> 01:22:50,128

at least put it up for approval, similarly to the GE salmon.

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01:22:50,128 --> 01:22:52,399

This doesn't serve as any medicinal purposes for

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01:22:52,399 --> 01:22:54,260

humans such as the case study.

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01:22:54,260 --> 01:22:57,806

Will it go through the same process as a new animal drug,

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01:22:57,806 --> 01:23:01,358

despite the fact that this is not a human or animal drug?

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01:23:01,358 --> 01:23:02,278

>> Dr. Barbero >> Okay thank you.

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01:23:02,278 --> 01:23:02,858

You got this?

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01:23:02,858 --> 01:23:06,748

>> Jason Dietz >> So, what I can focus on here today is the case study that's in front of us.

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01:23:06,748 --> 01:23:10,415

And what I can explain is that, in this particular case study,

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01:23:10,415 --> 01:23:12,766

the new animal drug provision was used,

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01:23:12,766 --> 01:23:18,092

because the recombinant DNA construct in the animal fits the definition of a new animal drug,

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01:23:18,092 --> 01:23:21,928

because it affects the structure or function of that new animal.

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01:23:21,928 --> 01:23:26,954

And it's the structure or function of that new animal drug definition is why it

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01:23:26,954 --> 01:23:31,996

gives us the authority to regulate this under the new animal drug provisions.

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01:23:35,138 --> 01:23:36,658

>> Dr. Barbero >> Yes, two questions over here.

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01:23:36,658 --> 01:23:38,878

So we'll start with the woman in the front row.

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01:23:38,878 --> 01:23:41,104

If you could say your name and your question, and

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01:23:41,104 --> 01:23:43,618

then we'll go to the gentleman next, in the next row.

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01:23:43,618 --> 01:23:48,691

>> Okay, Sally Fox, and my question is, what is in place to

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01:23:48,691 --> 01:23:53,678

evaluate how the animal is affected by this insertion.

1259  
01:23:53,678 --> 01:23:55,138  
The welfare of the animal.

1260  
01:23:57,558 --> 01:23:58,118  
>> Dr. Barbero >> Jason?

1261  
01:23:58,118 --> 01:23:58,958  
>> Jason Dietz >> Great question.

1262  
01:23:58,958 --> 01:24:03,475  
In fact, one of the aspects of this, as a new animal drug, the agency looks

1263  
01:24:03,475 --> 01:24:07,948  
to make sure, that the substance is actually safe for the animal itself.

1264  
01:24:07,948 --> 01:24:09,808  
It looks at the health of the animal.

1265  
01:24:12,608 --> 01:24:16,705  
>> Dr. Barbero >> And do you have it to the extent that you're able to talk  
about what some of

1266  
01:24:16,705 --> 01:24:19,203  
those questions might be that you can draw?

1267  
01:24:19,203 --> 01:24:23,208  
I'm assuming the GFI 187 provides some of the-

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01:24:23,208 --> 01:24:23,828  
>> Jason Dietz >> Absolutely.

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01:24:23,828 --> 01:24:24,848  
>> Dr. Barbero >> Those lines of questioning.

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01:24:24,848 --> 01:24:28,314  
>> Jason Dietz >> GFI 187 would be- >> Dr. Barbero >> Do you have any of those  
you can

1271  
01:24:28,314 --> 01:24:29,428  
elaborate on here?

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01:24:29,428 --> 01:24:30,568

Do you think that's the best place to go?

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01:24:30,568 --> 01:24:31,768

>> Jason Dietz >> I would say that's the best place to go.

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01:24:31,768 --> 01:24:34,607

>> Dr. Barbero >> Okay so if you look at that FDA's guidance for

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01:24:34,607 --> 01:24:38,194

industry 187 which is the document referred to here,

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01:24:38,194 --> 01:24:43,053

you can find the types of information that the agency would have regarding how

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01:24:43,053 --> 01:24:46,738

the health of the animal would be evaluated based on that.

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01:24:46,738 --> 01:24:50,376

>> Jason Dietz >> The other point there too is remember that the safety assessment is safe and

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01:24:50,376 --> 01:24:51,018

effective.

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01:24:51,018 --> 01:24:54,238

And here what we're talking about safe is safe for the animal,

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01:24:54,238 --> 01:24:57,579

and of course if it's a production animal, safe with the food and

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01:24:57,579 --> 01:24:59,916

any feed products from it be safe for humans.

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01:24:59,916 --> 01:25:03,070

But in general, you're saying is it safe for the animal?

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01:25:03,070 --> 01:25:07,188

So there's absolutely an animal safety component to this.

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01:25:07,188 --> 01:25:10,488

CVM takes that very seriously.

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01:25:10,488 --> 01:25:12,308

Hi, good morning, I'm Arturo.

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01:25:12,308 --> 01:25:16,460

I'm just curious as to how the FDA oversight would change

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01:25:16,460 --> 01:25:20,699

if the recombinant protein expressed was, for example,

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01:25:20,699 --> 01:25:25,390

a cow casein for food products as opposed to an insulin as a drug.

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01:25:28,020 --> 01:25:33,388

>> Jason Dietz >> So if it were a casein product instead of insulin as I understand it.

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01:25:33,388 --> 01:25:36,494

>> Dr. Barbero >> So the question is if it's casein that's being produced instead of

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01:25:36,494 --> 01:25:37,318

insulin, okay.

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01:25:37,318 --> 01:25:41,698

>> Jason Dietz >> Well, it may depend a bit also on the intended use of the casein.

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01:25:41,698 --> 01:25:43,118

That would be an important factor.

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01:25:43,118 --> 01:25:47,378

Is it intended for medicinal use, is it intended for food use?

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01:25:47,378 --> 01:25:49,718

We would take that into account.

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01:25:49,718 --> 01:25:53,548

And you would still also have your new animal drug components.

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01:25:53,548 --> 01:25:56,732

I think that's probably as much as I can

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01:25:56,732 --> 01:26:00,408

elaborate on that without a lot more detail.

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01:26:00,408 --> 01:26:05,098

>> Dr. Barbero >> So this is an example of where the conversation would be with FDA.

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01:26:05,098 --> 01:26:10,234

Where the product developer would say here is the exact product details and

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01:26:10,234 --> 01:26:12,198

the intended application.

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01:26:12,198 --> 01:26:14,755

>> Jason Dietz >> And I think, Robbie, that that's an important point, and

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01:26:14,755 --> 01:26:17,915

I mentioned that point quite a bit with plants, but the very same is true for

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01:26:17,915 --> 01:26:19,438

genetically engineered animals.

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01:26:19,438 --> 01:26:24,101

It is very very important to contact the agency early in development,

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01:26:24,101 --> 01:26:29,316

because they can help make sure that you are meeting your legal obligations and

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01:26:29,316 --> 01:26:32,018

help ensure that you are on a good track.

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01:26:32,018 --> 01:26:36,117

So I would strongly encourage folks to reach out to the folks at the Center for

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01:26:36,117 --> 01:26:40,348

Veterinary Medicine when they're interested in producing a new genetically

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01:26:40,348 --> 01:26:41,518

engineered animal.

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01:26:41,518 --> 01:26:43,458

>> Dr. Barbero >> So, did we have one in the back corner?

1313  
01:26:43,458 --> 01:26:46,838  
And then we'll do over here.

1314  
01:26:46,838 --> 01:26:47,858  
Name, please.

1315  
01:26:47,858 --> 01:26:49,178  
>> Sorry, Pablo Rose.

1316  
01:26:49,178 --> 01:26:52,140  
I'm faculty at UC Davis.

1317  
01:26:52,140 --> 01:26:56,998  
My question a little bit of a tweak to the way that this animal is constructed.

1318  
01:26:56,998 --> 01:26:59,063  
Instead of using a construct,

1319  
01:26:59,063 --> 01:27:04,226  
say let's take the very few differences between the primate insulin gene and

1320  
01:27:04,226 --> 01:27:09,071  
the human insulin gene are maybe a few base pairs], maybe 10, 20,

1321  
01:27:09,071 --> 01:27:13,940  
but we change those without using any recombinant product or material.

1322  
01:27:13,940 --> 01:27:17,146  
Would that still be considered an animal drug?

1323  
01:27:19,678 --> 01:27:22,838  
>> Jason Dietz >> I think I understand your question,  
however,

1324  
01:27:22,838 --> 01:27:26,735  
what I would suggest is back to the point I just mentioned.

1325  
01:27:26,735 --> 01:27:30,415  
That's an excellent kind of question to come to the agency and

1326  
01:27:30,415 --> 01:27:34,748  
talk to them about and get the experts' views on your specific product.

1327  
01:27:40,118 --> 01:27:43,146  
>> Yes, Kenneth Loy from MIT.

1328  
01:27:43,146 --> 01:27:47,099  
The question that I have is really on the issue of safety and

1329  
01:27:47,099 --> 01:27:50,257  
efficacy from the perspective of the rabbit.

1330  
01:27:50,257 --> 01:27:56,734  
If we look at this example and view this in the context of other therapeutics.

1331  
01:27:56,734 --> 01:28:02,858  
You'd be expecting potentially issues to emerge over longer periods of time.

1332  
01:28:02,858 --> 01:28:07,257  
If you look at the Japanese PMDA on regenerative medicines or

1333  
01:28:07,257 --> 01:28:11,657  
you look at the European Medicines Agency on therapeutics,

1334  
01:28:11,657 --> 01:28:16,575  
they're experimenting with adaptive pathways precisely because

1335  
01:28:16,575 --> 01:28:19,868  
it may take time for effects to materialize.

1336  
01:28:19,868 --> 01:28:24,894  
So what are the specific provisions in 187 for adaptation and

1337  
01:28:24,894 --> 01:28:29,278  
learning and observation over longer periods of time?

1338  
01:28:29,278 --> 01:28:34,567  
>> Jason Dietz >> That I would consider, in a scientific way,

1339  
01:28:34,567 --> 01:28:37,358  
a very weedy question.

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01:28:37,358 --> 01:28:42,500

Guidance 187 has a lot of detail in it but it is fairly broad.

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01:28:42,500 --> 01:28:47,738

That's probably a question, to be honest, best addressed to our experts back home.

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01:28:47,738 --> 01:28:50,581

If you wanna see me at the break, I'd be happy to tend to get a question back.

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01:28:50,581 --> 01:28:53,667

But I don't wanna give you an inadequate response, and

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01:28:53,667 --> 01:28:57,554

I think our folks back home will be able to give you the best response.

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01:28:57,554 --> 01:28:58,114

Thank you.

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01:28:58,114 --> 01:29:02,758

>> Dr. Barbero >> I will say broadly that if you look at the correlative framework in

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01:29:02,758 --> 01:29:08,162

the 1992 update, there is a principle that is articulated in those and

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01:29:08,162 --> 01:29:13,070

it was included in the slide that I presented at the beginning.

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01:29:13,070 --> 01:29:17,326

Talking about, encouraging the agencies to

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01:29:17,326 --> 01:29:22,366

continue to update their oversight of the products of

1351

01:29:22,366 --> 01:29:27,446

biotechnology as the science evolves in this space.

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01:29:27,446 --> 01:29:32,590

So that is certainly an underlying principle to the exist here and

1353  
01:29:32,590 --> 01:29:35,968  
how it relates to a specific product area.

1354  
01:29:35,968 --> 01:29:38,760  
I think that's best you talk to the agency about that.

1355  
01:29:40,950 --> 01:29:42,428  
We have time for one more on this.

1356  
01:29:42,428 --> 01:29:46,998  
Otherwise, we're gonna move on to our next case study.

1357  
01:29:46,998 --> 01:29:50,196  
One more over there, okay.

1358  
01:29:50,196 --> 01:29:52,268  
>> Vig Ganapathy >> Vig Ganapathy with the Everylife Foundation.

1359  
01:29:52,268 --> 01:29:57,269  
I'm curious about how the process at CBM informs the new

1360  
01:29:57,269 --> 01:30:01,953  
drug application process at CDER and whether any of

1361  
01:30:01,953 --> 01:30:07,400  
the determinations need to be included in the application.

1362  
01:30:08,420 --> 01:30:09,400  
>> Jason Dietz >> Good question.

1363  
01:30:09,400 --> 01:30:13,040  
In some instances, there may be, for example, in this case study, there may be

1364  
01:30:14,460 --> 01:30:18,860  
information about the milk that is relevant to both CDER and CVM.

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01:30:18,860 --> 01:30:23,916  
So there are mechanisms for the agency or the centers rather, to communicate

1366  
01:30:23,916 --> 01:30:28,531  
in some of the cases the data that suit one purpose may suit another as well.

1367  
01:30:28,531 --> 01:30:29,690  
But

1368  
01:30:29,690 --> 01:30:34,018  
again, I mean that would all depend upon the specific product that you have.

1369  
01:30:34,018 --> 01:30:38,898  
>> Dr. Barbero >> And typically the developer would need speaking with both of those centers.

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01:30:38,898 --> 01:30:40,619  
>> Jason Dietz >> Absolutely.  
>> Dr. Barbero >> In this case.

1371  
01:30:40,619 --> 01:30:45,193  
And when there are areas where information needs to be shared then that

1372  
01:30:45,193 --> 01:30:49,070  
would be done with all three of those parties at the table.

1373  
01:30:49,070 --> 01:30:54,028  
>> Jason Dietz >> Right, and I think one final point on this particular case study.

1374  
01:30:54,028 --> 01:30:57,749  
If you are used to producing new drugs and going with an IND,

1375  
01:30:57,749 --> 01:31:02,366  
it's useful to know that with a genetically engineered animal you should

1376  
01:31:02,366 --> 01:31:06,608  
be going to see CVM earlier in the process than you normally would for

1377  
01:31:06,608 --> 01:31:10,948  
an IND because you've got investigational new animal drug as well.

1378  
01:31:10,948 --> 01:31:14,848  
So again, once that lineage has been established you should go see CVM.

1379  
01:31:14,848 --> 01:31:22,048  
So, do not wait to go see CVM once you're ready to file IND, go well before that.

1380

01:31:22,048 --> 01:31:24,208

>> Dr. Barbero >> Okay, thank you for those great questions.

## Case Study: Microbial Products for Industrial Applications

1381

01:31:24,208 --> 01:31:29,628

The final case study is a microbial product for industrial application.

1382

01:31:29,628 --> 01:31:33,236

This is case study number seven in the handout that you have in front of you.

1383

01:31:35,858 --> 01:31:40,142

This is a hypothetical genetically engineered algae for biofuels.

1384

01:31:40,142 --> 01:31:43,695

A unicellular algae is genetically engineered with a plant

1385

01:31:43,695 --> 01:31:48,395

pest component to produce industrial oils for conversions into bio-fuels.

1386

01:31:48,395 --> 01:31:52,834

The product is a eukaryotic microalgae *Chlamydomonas reinhardtii*.

1387

01:31:52,834 --> 01:31:57,168

It's genetically engineered to produce an enzyme that increases lipid biosynthesis.

1388

01:31:57,168 --> 01:32:00,238

The extracted oils are later converted into biodiesel.

1389

01:32:00,238 --> 01:32:04,729

The enzyme that increases lipid production was originally isolated from the soybean

1390

01:32:04,729 --> 01:32:05,360

*Glycine max*.

1391

01:32:05,360 --> 01:32:09,955

The soybean gene is controlled by the cauliflower mosaic virus derived 35S

1392

01:32:09,955 --> 01:32:10,468

promoter.

1393

01:32:10,468 --> 01:32:12,775

The plasmid encoding the enzyme promoter and

1394

01:32:12,775 --> 01:32:17,289

selection marker is introduced into the algae through electroporation.

1395

01:32:17,289 --> 01:32:20,530

*C. reinhardtii* will be cultivated in an open pond system.

1396

01:32:20,530 --> 01:32:23,928

The remnants of the micro algae are intended for use as fish food.

1397

01:32:23,928 --> 01:32:26,148

Which agencies have oversight and why?

1398

01:32:26,148 --> 01:32:29,411

The USDA has oversight because the micro algae are engineered with a plant

1399

01:32:29,411 --> 01:32:30,208

pest component.

1400

01:32:30,208 --> 01:32:33,928

The Cauliflower Mosaic Virus S35 promoter.

1401

01:32:33,928 --> 01:32:38,457

EPA has oversight because the micro algae are engineered for

1402

01:32:38,457 --> 01:32:42,631

industrial use with genes outside the genus *Chlamydomonas* and

1403

01:32:42,631 --> 01:32:48,338

as such it fall under rules implementing the Toxic Substances Control Act.

1404

01:32:48,338 --> 01:32:53,455

And the FDA will have oversight because

1405

01:32:53,455 --> 01:32:59,198

the microalgae will be used for animal food.

1406

01:32:59,198 --> 01:32:59,758

Okay, Mark.

1407  
01:33:02,973 --> 01:33:06,530  
>> Dr. Segal >> Okay. I'll go first.

1408  
01:33:06,530 --> 01:33:07,650  
>> Dr. Barbero >> Are you not first, Mark?

1409  
01:33:10,860 --> 01:33:12,150  
>> Dr. Segal >> I'm not sure.

1410  
01:33:12,150 --> 01:33:13,218  
Originally it was Neil.

1411  
01:33:13,218 --> 01:33:14,619  
>> Dr. Barbero >> Okay, Neil, go ahead.

1412  
01:33:14,619 --> 01:33:16,140  
>> Dr. Hoffman >> Okay.

1413  
01:33:16,140 --> 01:33:23,568  
So The USDA role would be very similar to what I've described in the other cases.

1414  
01:33:23,568 --> 01:33:28,846  
I've just mentioned that this case, this is GE algae in an

1415  
01:33:28,846 --> 01:33:33,608  
open pond situation we've never regulated before.

1416  
01:33:33,608 --> 01:33:41,049  
So the main difference here is that at the time of an environmental release,

1417  
01:33:41,049 --> 01:33:45,467  
we may find that there's an exception to this

1418  
01:33:45,467 --> 01:33:50,121  
confined field trial categorical exclusion,

1419  
01:33:50,121 --> 01:33:54,539  
and the exception we make is for new species or

1420  
01:33:54,539 --> 01:33:59,542  
novel modifications that raise new issues since we

1421  
01:33:59,542 --> 01:34:04,760  
have never regulated an algae in this situation.

1422  
01:34:04,760 --> 01:34:09,713  
There's a good possibility that we would decide to do an environmental

1423  
01:34:09,713 --> 01:34:12,931  
assessment at the time of the field trial, and

1424  
01:34:12,931 --> 01:34:17,816  
otherwise this is very similar to what we've done in the other cases.

1425  
01:34:20,988 --> 01:34:27,231  
>> Dr. Segal >> Okay so as Robbie said, this is a microbe that's used for a

1426  
01:34:27,231 --> 01:34:31,668  
purpose that's not excluded by TSCA.

1427  
01:34:31,668 --> 01:34:36,317  
It's considered new because its genes come from more than one genus,

1428  
01:34:36,317 --> 01:34:38,299  
which we call intergeneric.

1429  
01:34:39,770 --> 01:34:45,916  
So if this microorganism is used in a contained structure and

1430  
01:34:45,916 --> 01:34:53,991  
it complies with the list of best practices of our current regulation,

1431  
01:34:53,991 --> 01:34:59,068  
no reporting to the EPA at that stage is required.

1432  
01:34:59,068 --> 01:35:02,346  
Structure is interpreted broadly by EPA.

1433  
01:35:02,346 --> 01:35:07,288  
We're not just talking about a lab bench in a building.

1434  
01:35:07,288 --> 01:35:12,279  
For algae this is important because photobioreactors

1435  
01:35:12,279 --> 01:35:16,408  
could be included as contained structures.

1436  
01:35:16,408 --> 01:35:20,836  
Of course, that means that all the piping and

1437  
01:35:20,836 --> 01:35:24,940  
all the ancillary materials associated with

1438  
01:35:24,940 --> 01:35:29,158  
photobioreactor have to be truly contained.

1439  
01:35:29,158 --> 01:35:33,416  
So if there isn't any question about the design of

1440  
01:35:33,416 --> 01:35:38,857  
the structure as Jason has been saying all along, we agree.

1441  
01:35:38,857 --> 01:35:43,143  
Please contact us, talk to us and

1442  
01:35:43,143 --> 01:35:48,347  
we can go through some of the details to be

1443  
01:35:48,347 --> 01:35:56,171  
sure that there is no need to provide any formal report list.

1444  
01:35:56,171 --> 01:36:00,712  
So EPA does not separate small-scale from large-scale in

1445  
01:36:00,712 --> 01:36:05,100  
determining whether there is a need for oversight.

1446  
01:36:05,100 --> 01:36:11,030  
A release is a release, and thus a TSCA experimental release application,

1447  
01:36:11,030 --> 01:36:15,720  
a TERA, would be needed as long as there is an intended release.

1448  
01:36:15,720 --> 01:36:19,590  
This is intended for an open pond system.

1449

01:36:19,590 --> 01:36:24,340

Presumably, somebody will be testing this in an open pond.

1450

01:36:24,340 --> 01:36:27,434

And Robbie, could you go back to the image?

1451

01:36:29,487 --> 01:36:34,033

And let's see if I can borrow this because I

1452

01:36:34,033 --> 01:36:38,331

want to show you a little bit about scale.

1453

01:36:38,331 --> 01:36:42,903

Back here are some mini ponds that are basically

1454

01:36:42,903 --> 01:36:46,340

something like a thousand liters.

1455

01:36:47,780 --> 01:36:51,420

Then it can go up to something that's about twice the size and

1456

01:36:51,420 --> 01:36:53,060

something that's quite bit larger.

1457

01:36:53,060 --> 01:36:58,220

All of which are found in one particular facility,

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01:36:58,220 --> 01:37:00,580

in this case a test bed in Arizona,

1459

01:37:00,580 --> 01:37:05,820

which might be a kind of place where an experimental release could take place.

1460

01:37:05,820 --> 01:37:11,270

Beyond these sizes, somebody may want to then go five, ten times

1461

01:37:11,270 --> 01:37:16,860

as large out in the middle of the desert someplace to do their experimentation

1462

01:37:16,860 --> 01:37:23,530

to make sure that their organism works on something approaching a commercial scale.

1463

01:37:24,680 --> 01:37:30,850

All of these could be wrapped up into one single TERA.

1464

01:37:30,850 --> 01:37:35,830

But if anything goes wrong, or changes, or something shows up in the course of

1465

01:37:35,830 --> 01:37:41,120

doing experimentation as one goes up in scale,

1466

01:37:41,120 --> 01:37:45,590

it might not have been covered by the data supplied to us ---

1467

01:37:45,590 --> 01:37:49,000

all those kinds of data I described earlier.

1468

01:37:49,000 --> 01:37:53,680

It might not have been described well enough to support

1469

01:37:55,410 --> 01:37:59,650

an acceptance of going forward with

1470

01:37:59,650 --> 01:38:05,150

that particular TSCA experimental release application for all the scales.

1471

01:38:05,150 --> 01:38:11,340

So, what we might expect to see in a case like this would be a progression.

1472

01:38:11,340 --> 01:38:19,330

A succession of individual TERAs over the course of different growing seasons and

1473

01:38:19,330 --> 01:38:24,529

different scales that are appropriate for this particular microorganism.

1474

01:38:26,200 --> 01:38:31,262

Assuming everything goes well with this experimentation,

1475

01:38:31,262 --> 01:38:36,420

the data that are gathered from the experimentation are gonna

1476

01:38:36,420 --> 01:38:41,298

be useful later on for evaluation of commercialization.

1477

01:38:41,298 --> 01:38:49,682

Then presume the submitter would want to make some money off of this,

1478

01:38:49,682 --> 01:38:54,534

and they would have to then come to us for

1479

01:38:54,534 --> 01:38:59,242

a Microbial Mommercial, excuse me,

1480

01:38:59,242 --> 01:39:05,735

MCAN, Microbial Commercial Application Notification.

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01:39:05,735 --> 01:39:07,717

So in the case of the TERA,

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01:39:07,717 --> 01:39:13,260

we have to formally give an approval before they can go forward.

1483

01:39:13,260 --> 01:39:18,960

In the case of an MCAN, we do a review regardless.

1484

01:39:18,960 --> 01:39:23,835

If something is new, it triggers oversight, and

1485

01:39:23,835 --> 01:39:26,973

so we would go through a review.

1486

01:39:26,973 --> 01:39:31,395

If at the end of the review we find that there are no issues ---

1487

01:39:31,395 --> 01:39:36,360

that we cannot make a finding that there is an unreasonable risk to

1488

01:39:36,360 --> 01:39:40,873

manner the environment --- all we have to do is stay silent and

1489

01:39:40,873 --> 01:39:45,657

after 90 days, the submitter is permitted to go through with

1490

01:39:45,657 --> 01:39:49,670

whatever commercial activities they choose to do.

1491

01:39:50,680 --> 01:39:58,955

Now let's say this submitter said we want to make this organism at one site.

1492

01:39:58,955 --> 01:40:03,170

We want to have one particular use making biodiesel and that's it.

1493

01:40:04,280 --> 01:40:09,330

We have to consider that somebody else may choose to

1494

01:40:09,330 --> 01:40:13,620

produce the same organisms somewhere else, or for a different purpose.

1495

01:40:13,620 --> 01:40:17,990

So we have to think of all the plausible uses for the organism,

1496

01:40:17,990 --> 01:40:24,560

all the plausible production methodologies, and consider risks overall.

1497

01:40:24,560 --> 01:40:29,590

We may find that we're uncomfortable with saying nothing.

1498

01:40:29,590 --> 01:40:33,827

And that we believe that there should be some

1499

01:40:33,827 --> 01:40:38,866

limitations on the production from a risk basis, or

1500

01:40:38,866 --> 01:40:44,374

production or use of whatever commercial application.

1501

01:40:44,374 --> 01:40:50,007

We can and would then consider working with the submitter

1502

01:40:50,007 --> 01:40:56,108

to make sure that there are appropriate limitations for

1503  
01:40:56,108 --> 01:41:00,700  
that production or use of the microorganism.

1504  
01:41:02,130 --> 01:41:05,360  
Then a Consent Order would be drawn up.

1505  
01:41:05,360 --> 01:41:10,604  
And the submitter would agree to these conditions, and therefore

1506  
01:41:10,604 --> 01:41:16,890  
limitations would be placed on the commercialization of this microorganism.

1507  
01:41:19,090 --> 01:41:26,740  
It's entirely possible that additional data could reveal that additional uses,

1508  
01:41:26,740 --> 01:41:32,170  
or just additional production of different sites, might be appropriate.

1509  
01:41:32,170 --> 01:41:33,990  
And the submitter might choose,

1510  
01:41:33,990 --> 01:41:37,942  
through maybe additional TERAs, to gather that information.

1511  
01:41:37,942 --> 01:41:42,800  
Provide it to us and provide us with reasons so

1512  
01:41:42,800 --> 01:41:46,600  
that we could lift some of those limitations, or all of the limitations.

1513  
01:41:46,600 --> 01:41:51,912  
That is part of our process.

1514  
01:41:51,912 --> 01:41:56,730  
It's also possible that we may find that we have to

1515  
01:41:56,730 --> 01:42:00,525  
unilaterally impose limitations.

1516  
01:42:00,525 --> 01:42:03,725  
We prefer that we don't do this.

1517

01:42:03,725 --> 01:42:07,685

In this case, we're only increasing the production

1518

01:42:07,685 --> 01:42:09,135

of a natural-

>> Dr. Barbero >> Mark,

1519

01:42:09,135 --> 01:42:10,925

I'm gonna just try to get you to wrap up.

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01:42:10,925 --> 01:42:11,462

>> Dr. Segal >> Last sentence.

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01:42:11,462 --> 01:42:12,978

>> Dr. Barbero >> Okay, good.

>> Okay, so

1522

01:42:12,978 --> 01:42:17,738

if there is no new chemical being produced,

1523

01:42:17,738 --> 01:42:23,794

then there will not be a need for additional oversight.

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01:42:23,794 --> 01:42:28,577

If, in fact, they were making this organism produce a chemical that it didn't

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01:42:28,577 --> 01:42:33,511

naturally produce, and that was not on our inventory of chemical substances,

1526

01:42:33,511 --> 01:42:36,676

a separate review of the chemical would be needed,

1527

01:42:36,676 --> 01:42:40,680

a Premanufacturing Notification would have to be supplied.

1528

01:42:42,710 --> 01:42:43,520

>> Dr. Barbero >> Jason.

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01:42:43,520 --> 01:42:47,720

>> Jason Dietz >> Sure, and if the spent algae were to be used for animal feed,

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01:42:47,720 --> 01:42:52,030

again it would have to be safe and lawful for its use as animal feed.

1531

01:42:52,030 --> 01:42:56,240

One of the considerations would be whether, for instance,

1532

01:42:56,240 --> 01:43:01,440

the algae had aspects to it such as remnants of the fermentation material or

1533

01:43:01,440 --> 01:43:04,990

the substances produced during fermentation, or

1534

01:43:04,990 --> 01:43:08,724

substances added to the fermentation to control it.

1535

01:43:08,724 --> 01:43:13,667

Whether those substances present in the spent algae would be important

1536

01:43:13,667 --> 01:43:16,973

to consider in terms of safety for animal feed.

1537

01:43:16,973 --> 01:43:21,825

And all those factors would be considered in whether something like this

1538

01:43:21,825 --> 01:43:26,420

would require a food additive petition or whether it would not.

1539

01:43:26,420 --> 01:43:29,701

And so this is a great example of the desire or

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01:43:29,701 --> 01:43:33,706

the need to consult the agency early in development.

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01:43:33,706 --> 01:43:35,965

And in particular, for things like this,

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01:43:35,965 --> 01:43:40,046

it's useful to think about your product life cycle very early in research and

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01:43:40,046 --> 01:43:43,437

development, so that you are consulting with the agency before

1544  
01:43:43,437 --> 01:43:47,305  
you have a lot of spent algae that you are looking to get rid of in some way.

1545  
01:43:47,305 --> 01:43:50,787  
So again, think ahead, and come and talk to the agency

1546  
01:43:50,787 --> 01:43:55,114  
about things like this because this is where we can be very helpful.

1547  
01:43:55,114 --> 01:44:00,171  
Perhaps, it's something as simple as a tweak to fermentation conditions,

1548  
01:44:00,171 --> 01:44:05,333  
may mean, A regulatory hurdle versus something that is much less of a hurdle.

1549  
01:44:05,333 --> 01:44:06,566  
Thank you.  
>> Dr. Barbero >> Great.

## Case Study Q&A Microbial Products for Industrial Applications

1550  
01:44:06,566 --> 01:44:15,080  
So, let's do questions on this case study right up here at the front.

1551  
01:44:15,080 --> 01:44:17,390  
Why don't you just go ahead and we'll start with you and then I can repeat it.

1552  
01:44:17,390 --> 01:44:18,551  
>> Okay sure.

1553  
01:44:18,551 --> 01:44:21,976  
My name is Alan and I have a question.

1554  
01:44:21,976 --> 01:44:30,630  
I there a difference if you [INAUDIBLE]

1555  
01:44:30,630 --> 01:44:35,097  
an algae [INAUDIBLE]

1556  
01:44:35,097 --> 01:44:39,850  
versus [INAUDIBLE]?

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01:44:39,850 --> 01:44:42,250

>> Dr. Barbero >> So Mark, why don't you start.

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01:44:42,250 --> 01:44:46,538

So the question is whether if the product being

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01:44:46,538 --> 01:44:51,310

produced is expressed- >> Alan >> Transient.

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01:44:51,310 --> 01:44:53,360

>> Dr. Barbero >> So if the expression level varies over time.

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01:44:53,360 --> 01:44:57,340

>> Dr. Segal >> So that would be part of our consideration during the course of our

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01:44:57,340 --> 01:45:02,260

risk assessment, whether that transient production would have an effect

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01:45:02,260 --> 01:45:05,380

on the environment, for example.

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01:45:08,260 --> 01:45:13,730

And it's just a specific part of the assessment, would

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01:45:13,730 --> 01:45:19,790

be case-specific, and we would just have to evaluate that question in detail.

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01:45:19,790 --> 01:45:22,390

I can't give you a yes or no answer right now.

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01:45:24,660 --> 01:45:26,230

>> Dr. Barbero >> Anybody else?  
Jason?

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01:45:26,230 --> 01:45:28,380

>> Jason Dietz >> Yeah, I think Mark's point is very good.

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01:45:28,380 --> 01:45:33,550

I mean, for us usually it would depend upon what in fact is going into the food,

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01:45:33,550 --> 01:45:35,940

or the feed, and what is its state at that point, and

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01:45:35,940 --> 01:45:39,740

what comes along with it as residual material?

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01:45:39,740 --> 01:45:42,525

I think again, It's a good question to come and

1573

01:45:42,525 --> 01:45:46,229

talk to us about because the specifics there may be important.

1574

01:45:46,229 --> 01:45:47,204

>> Dr. Barbero >> Yep.

1575

01:45:47,204 --> 01:45:49,154

Thank you, yes?

1576

01:45:49,154 --> 01:45:51,430

>> Dana Perls >> Hi, thank you, another question.

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01:45:51,430 --> 01:45:52,371

>> Dr. Barbero >> Name please?

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01:45:52,371 --> 01:45:53,149

>> Dana Perls.

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01:45:53,149 --> 01:45:54,426

>> Dr. Barbero >> Okay.

1580

01:45:54,426 --> 01:45:57,790

>> Dana Perls >> So I have a question about containment.

1581

01:45:57,790 --> 01:46:01,980

Earlier you addressed the difference between confinement and containment.

1582

01:46:01,980 --> 01:46:06,142

And in this case, and in the case of a lot of algal biofuels,

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01:46:06,142 --> 01:46:11,727

genetically engineered using transgenics or newer gene editing techniques,

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01:46:11,727 --> 01:46:17,252

it's questionable whether or not containment is ever a 100% effective.

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01:46:17,252 --> 01:46:22,647

And so you mentioned that containment, that you try to ensure

1586

01:46:22,647 --> 01:46:27,434

that it's the probability of escape is close to zero.

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01:46:27,434 --> 01:46:30,231

But in the case of both open tanks and

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01:46:30,231 --> 01:46:35,870

also containment that might just be plastic bags or other forms.

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01:46:35,870 --> 01:46:40,530

What is the process to ensure that there is no escape, and

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01:46:40,530 --> 01:46:44,950

in the case that even minimal escape,

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01:46:44,950 --> 01:46:50,300

even if it is close to zero, that may have significant environmental impacts.

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01:46:50,300 --> 01:46:51,870

How do you address those?

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01:46:51,870 --> 01:46:54,470

>> Dr. Barbero >> So, I think it's important to note that the discussion about containment and

1594

01:46:54,470 --> 01:46:56,660

confinement at the beginning, was from USDA.

1595

01:46:56,660 --> 01:47:03,006

And that was a discussion about that there was not specific to the algae,

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01:47:03,006 --> 01:47:07,184

and then there was, EPA also has confinement.

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01:47:07,184 --> 01:47:09,506

That's let's let Mark handle it.

1598

01:47:09,506 --> 01:47:12,940

>> Dr. Segal >> Yeah, so we don't use the term confined.

1599

01:47:14,270 --> 01:47:15,460

>> Dr. Barbero >> EPA does not.

1600

01:47:15,460 --> 01:47:20,669

>> Dr. Segal >> No, but you are asking a very good question, which would be the kind of

1601

01:47:23,010 --> 01:47:28,070

question we would be asking when somebody would be consulting with us

1602

01:47:28,070 --> 01:47:33,550

to inquire whether or not their particular system is truly contained.

1603

01:47:33,550 --> 01:47:36,170

We would expect to see some kind of data or

1604

01:47:36,170 --> 01:47:42,310

information that would establish whether or not something is completely contained.

1605

01:47:42,310 --> 01:47:46,765

We're looking for secondary containment in case there are leaks.

1606

01:47:46,765 --> 01:47:51,709

Things like berms and collection of material or fluids or

1607

01:47:51,709 --> 01:47:55,320

something like that, that might come out. ...

1608

01:47:55,320 --> 01:48:00,577

Or use in a desert environment where escape

1609

01:48:00,577 --> 01:48:08,410

is not in the immediate area of the production can be controlled.

1610

01:48:08,410 --> 01:48:14,020

If in fact, that is an approach is something somebody might want to take.

1611  
01:48:14,020 --> 01:48:16,400  
So yes that's an interesting question but

1612  
01:48:16,400 --> 01:48:21,380  
it is something we would evaluate if somebody would come to us beforehand.

1613  
01:48:21,380 --> 01:48:27,070  
>> Dr. Barbero >> And Neil, would USDA be addressing those in this specific case?

1614  
01:48:27,070 --> 01:48:28,086  
>> Dr. Hoffman >> It's possible.

1615  
01:48:28,086 --> 01:48:32,679  
We have permitted some field trials of

1616  
01:48:32,679 --> 01:48:37,855  
algae that was grown like you were saying.

1617  
01:48:37,855 --> 01:48:41,310  
We sent someone out to the site and looked at it.

1618  
01:48:41,310 --> 01:48:45,410  
It was basically in a desert environment and

1619  
01:48:45,410 --> 01:48:51,250  
we felt that if there was a breach of that contained

1620  
01:48:52,400 --> 01:48:56,610  
bioreactor that the algae could not grow in that environment.

1621  
01:48:58,170 --> 01:48:59,690  
So, that's how we considered it.

1622  
01:48:59,690 --> 01:49:04,410  
>> Dana Perls >> And so the regulations for what's considered to be closed containment and

1623  
01:49:04,410 --> 01:49:09,990  
open containment, given that containment isn't in fact a 100% effective,

1624

01:49:09,990 --> 01:49:12,870

do the regulations apply similarly whether closed or open?

1625

01:49:14,320 --> 01:49:16,780

>> Dr. Barbero >> So, is that question for USDA or for EPA?

1626

01:49:18,190 --> 01:49:19,190

>> Dana Perls >> Both, thank you.

1627

01:49:19,190 --> 01:49:21,911

>> Dr. Hoffman >> Well, in this particular case we did permit it.

1628

01:49:21,911 --> 01:49:24,120

So we were considering it.

1629

01:49:24,120 --> 01:49:25,583

>> Dr. Barbero >> Not in this case but in the one that you were [CROSSTALK].

1630

01:49:25,583 --> 01:49:27,046

>> Dr. Hoffman >> I'm sorry,

>> Dr. Barbero >> The previous one.

1631

01:49:27,046 --> 01:49:33,330

>> Dr. Hoffman >> The one you referred to of a bioreactor in an outdoor environment.

1632

01:49:33,330 --> 01:49:37,820

We did consider that confined and we did permit it.

1633

01:49:39,740 --> 01:49:42,630

We generally have used,

1634

01:49:42,630 --> 01:49:48,070

where we have not issued permits have generally been in greenhouse situations.

1635

01:49:50,250 --> 01:49:56,050

Yes, I suppose you could have some pollen escape from a greenhouse.

1636

01:49:56,050 --> 01:49:58,470

I mean, it requires-

>> Dr. Barbero >> But for algae.

1637

01:49:58,470 --> 01:50:03,411

>> Dr. Hoffman >> But for algae, we would not regulate algae, for

1638

01:50:03,411 --> 01:50:07,026

example, if it was a laboratory and

1639

01:50:07,026 --> 01:50:13,880

it was just bioreactors in a four wall environment like this.

1640

01:50:13,880 --> 01:50:16,830

>> Dr. Barbero >> So Mark, can you address how you think about containment in

1641

01:50:16,830 --> 01:50:17,779

maybe a little more detail.

1642

01:50:18,960 --> 01:50:22,990

>> Dr. Segal >> Yeah, I'm not sure I can do it in a lot more

1643

01:50:22,990 --> 01:50:27,980

detail because a lot of it is going to be depending upon the specifics.

1644

01:50:27,980 --> 01:50:33,130

We will have our engineers look at the production system.

1645

01:50:33,130 --> 01:50:39,599

If there's any question about whether something is contained,

1646

01:50:39,599 --> 01:50:45,370

and we have had cases already where people have come to us.

1647

01:50:46,930 --> 01:50:50,230

We do have some experience with algae, and

1648

01:50:50,230 --> 01:50:53,695

in both contained systems and open systems.

1649

01:50:53,695 --> 01:51:00,880

We will have people

1650

01:51:00,880 --> 01:51:07,350

developing ways to look at containment.

1651

01:51:07,350 --> 01:51:09,950

Right now we're poised to consider document, and

1652

01:51:09,950 --> 01:51:12,979

this is something I haven't had a chance to talk about yet.

1653

01:51:12,979 --> 01:51:19,428

But we're in the process of revising our Points to Consider document,

1654

01:51:19,428 --> 01:51:25,040

to include some specifics on dealing with algal production.

1655

01:51:25,040 --> 01:51:31,260

We're doing that right now so I can't give you any details.

1656

01:51:31,260 --> 01:51:35,730

We had a public meeting on this issue back in September and

1657

01:51:35,730 --> 01:51:40,950

we're dealing with some of those comments and issues at this time.

1658

01:51:42,760 --> 01:51:45,020

I guess I really can't answer more than that.

1659

01:51:45,020 --> 01:51:46,156

>> Dr. Barbero >> Great, thank you.

1660

01:51:46,156 --> 01:51:49,277

We have time for one more question.

1661

01:51:49,277 --> 01:51:52,528

Is it okay if we let somebody who hasn't asked yet?

1662

01:51:55,764 --> 01:51:59,220

>> Vince Sewalt >> Hi this is Vince Sewalt with Dupont.

1663

01:51:59,220 --> 01:52:00,680

Question for Jason.

1664

01:52:01,820 --> 01:52:08,050

You're, kind of, light on FDA requirements for the algae.

1665

01:52:08,050 --> 01:52:12,100

If they end up in animal feed as a feed ingredient,

1666

01:52:12,100 --> 01:52:16,009

it is likely that they would be considered a food additive.

1667

01:52:17,290 --> 01:52:22,330

So my experience is one would get in touch with CVM

1668

01:52:22,330 --> 01:52:25,570

very early in the process to verify that.

1669

01:52:25,570 --> 01:52:28,960

And then establish a plan for

1670

01:52:28,960 --> 01:52:33,620

either a GRAS determination as an exemption to a food additive.

1671

01:52:33,620 --> 01:52:36,498

So could you elaborate on that option for

1672

01:52:36,498 --> 01:52:41,290

GRAS determination.

1673

01:52:41,290 --> 01:52:45,520

>> Jason Dietz >> Well, the most I can really say is, again, it may depend upon the specifics

1674

01:52:45,520 --> 01:52:51,066

associated with the product and what our scientists at CVM come out.

1675

01:52:51,066 --> 01:52:55,078

But certainly, you're right, there is always the possibility that something

1676

01:52:55,078 --> 01:52:59,149

could be generally recognized as safe, and you could voluntarily submit a notice

1677

01:52:59,149 --> 01:53:02,337

indicating that your product is generally recognized as safe.

1678

01:53:02,337 --> 01:53:07,392

But I think you made, what I think is the excellent point, is that is,

1679

01:53:07,392 --> 01:53:12,452

think about this early in development because the regulatory process

1680

01:53:12,452 --> 01:53:17,190

may be important to your regulatory and development timelines.

1681

01:53:17,190 --> 01:53:20,790

And so I think really what I heard from your question

1682

01:53:20,790 --> 01:53:25,790

is primarily go talk the agencies earlier, early in the process.

1683

01:53:25,790 --> 01:53:29,300

Whether or not they would consider this particular substance a food additive or

1684

01:53:29,300 --> 01:53:31,980

a substance that is generally recognized as safe,

1685

01:53:31,980 --> 01:53:34,710

may hinge upon the specifics of the situation.

1686

01:53:34,710 --> 01:53:37,558

For example some oils may be harmful to certain animals,

1687

01:53:37,558 --> 01:53:38,931

while others it may not be.

1688

01:53:38,931 --> 01:53:43,291

And so it's very hard to make that specific case

1689

01:53:43,291 --> 01:53:47,330

without knowing down to the finest detail.

1690

01:53:47,330 --> 01:53:54,320

>> Dr. Segal >> And I would like to say amen to a what Jason said about coming to us early.

1691

01:53:54,320 --> 01:53:58,650

This would go to the dealing with, for example, the question that

1692  
01:53:58,650 --> 01:54:03,350  
was just asked about how do I know whether or not my system is contained?

1693  
01:54:03,350 --> 01:54:05,110  
Come to us first.

1694  
01:54:05,110 --> 01:54:10,290  
Ask us first before you start developing a system, or

1695  
01:54:10,290 --> 01:54:13,030  
get very far along with it.

1696  
01:54:13,030 --> 01:54:16,320  
>> Dr. Barbero >> Okay, so with that, we are finished with the case studies.

1697  
01:54:17,470 --> 01:54:20,560  
We will have a little bit of an adjustment to the agenda here in order to make sure

1698  
01:54:20,560 --> 01:54:21,640  
that we accomplish everything.

1699  
01:54:21,640 --> 01:54:23,590  
Do you wanna give an update on that Mike.

1700  
01:54:26,530 --> 01:54:30,960  
>> Dr. Firko >> So the bad news is we're about 25 minutes behind

1701  
01:54:30,960 --> 01:54:34,310  
The good news is we dropped a 25 minute session.

1702  
01:54:34,310 --> 01:54:36,570  
So we're right about where we need to be.

1703  
01:54:36,570 --> 01:54:37,810  
The break will start now.

1704  
01:54:37,810 --> 01:54:40,570  
It will run 11:30 to 11:50.

1705

01:54:40,570 --> 01:54:44,590

When you come back at 11:50 for the breakout session,

1706

01:54:44,590 --> 01:54:48,260

they will ask the full hour as in the agenda, and

1707

01:54:48,260 --> 01:54:53,580

then we should be able to start the public comment period as scheduled at 12:50.

1708

01:54:53,580 --> 01:54:56,730

So, the locations for the different break out groups.

1709

01:54:56,730 --> 01:55:00,030

The governance group will be in this room.

1710

01:55:00,030 --> 01:55:01,660

I would say on this side would be better,

1711

01:55:01,660 --> 01:55:04,940

because there's a monitor on the floor over here.

1712

01:55:04,940 --> 01:55:07,880

The communications break out will be in conference room

1713

01:55:07,880 --> 01:55:12,169

A which is just on the other side of the registration tables.

1714

01:55:13,730 --> 01:55:17,840

And the regulatory certainty will be in conference room B,

1715

01:55:17,840 --> 01:55:22,440

which is the one closest to the registration tables.

1716

01:55:22,440 --> 01:55:25,660

The hotel right over here has some salads that they sell.

1717

01:55:25,660 --> 01:55:27,620

And there's a food truck out this way.

1718

01:55:27,620 --> 01:55:30,470

And there's vending machines in various places if you'd like to get something to

1719

01:55:30,470 --> 01:55:31,630

eat in the next 20 minutes or so.

1720

01:55:35,480 --> 01:55:38,394

So we'll probably repeat this, but

1721

01:55:38,394 --> 01:55:42,351

the comments will be done in alphabetical order.

1722

01:55:42,351 --> 01:55:46,878

And we will have the listing in the room at the beginning of that session and

1723

01:55:46,878 --> 01:55:48,200

during the session.

1724

01:55:48,200 --> 01:55:50,799

So you can see when your comment will come up.

1725

01:55:54,258 --> 01:55:55,931

>> Dr. Barbero >> All right, thanks everybody.