

1 **Title: Atrazine and amphibians: Data re-analysis and a summary of the controversy**

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6 **Keywords:** amphibian, atrazine, conflicts of interest, disease, endocrine disruptor, frog,
7 herbicide, pesticide, Syngenta, toxicity, US Environmental Protection Agency

8

9 **Abstract.** The herbicide atrazine is one of the most commonly used, well studied, and
10 controversial pesticides on the planet. Much of the controversy involves the effects of atrazine
11 on wildlife, particularly amphibians and their non-infectious and infectious diseases, including
12 diseases caused by trematode infections. Here I re-analyze data from authors that were funded
13 by Syngenta Crop Protection, Inc., the company that produces atrazine, and show that even these
14 authors revealed that increasing concentrations of atrazine applied to outdoor mesocosms
15 increases the population growth rate of snails that can transmit trematode parasites to
16 amphibians. These researchers missed this finding in their data because they never calculated
17 population growth rates for the snail populations before they reached a carrying capacity or
18 crashed. These results demonstrate that both Syngenta-funded and non-Syngenta-funded
19 researchers have provided evidence that ecologically relevant concentrations of atrazine are
20 capable of increasing snail populations. Given the controversy surrounding the effects of
21 atrazine on amphibians, I follow this re-analysis with a timeline of some of the most salient
22 events in the history of the atrazine-amphibian controversy.

23 **Introduction**

24 The herbicide atrazine [2-chloro-4-(ethylamino)-6-(isopropylamino)-S-triazine] is one of
25 the most widely studied, commonly used, and controversial pesticides on the planet. A search
26 for the term “atrazine” in the search engine Web of Science (conducted on 11/17/2016) produced
27 11,203 studies. Atrazine was the most commonly used pesticide in the US before it was recently
28 surpassed by the herbicide glyphosate (Roundup®), which happened because of the advent of
29 genetically modified crops (Grube et al. 2011). Syngenta Crop Protection, Inc., the company
30 that produces atrazine, earns approximately \$2.5 billion annually from its selective herbicides, of
31 which atrazine is their leading product. Because of its heavy use, as well as its persistence and
32 mobility, atrazine is one of the most common chemical contaminants of freshwater and thus is
33 regularly found in habitats where many freshwater vertebrates, such as fish and amphibians,
34 develop (Rohr et al. 2003, Knutson et al. 2004). Consequently, there has been considerable
35 interest in the effects of atrazine on freshwater vertebrates (e.g. Solomon et al. 2008, Rohr and
36 McCoy 2010b), particularly amphibians because of their permeable skin and global declines
37 (Rohr et al. 2008a, Wake and Vredenburg 2008, Rohr and Raffel 2010, Liu et al. 2013, Raffel et
38 al. 2013, Rohr et al. 2015).

39 Research on the effects of atrazine on amphibians, however, has been highly contentious.
40 Much of the controversy on atrazine and amphibians involves the effects of atrazine on their
41 non-infectious diseases, such as disruption of the function and development of their endocrine
42 and reproductive systems, and infectious diseases, such as trematode infections. Authors funded
43 by Syngenta Crop Protection have argued that atrazine does not increase populations of snails
44 that can transmit trematodes to amphibians (Baxter et al. 2011), whereas non-Syngenta-funded
45 authors provide data suggesting that atrazine can increase snail populations (Rohr et al. 2008).

46 Here, I briefly review the effects of atrazine on amphibians. I then re-analyze the snail data
47 provided by authors that were funded by Syngenta Crop Protection, Inc. (Baxter et al. 2011).
48 Given the controversy surrounding the effects of atrazine on amphibians, I then follow this re-
49 analysis with a timeline of some of the most salient events in the history of the atrazine-
50 amphibian controversy.

51

52 **Background on the Effects of Atrazine on Amphibians**

53 Atrazine has a variety of effects on freshwater organisms, including fish and amphibians.
54 For example, atrazine has been reported to affect amphibian behaviors crucial for foraging,
55 predator avoidance (Rohr et al. 2003, 2004, Rohr et al. 2009), and desiccation resistance (Rohr
56 and Palmer 2005, 2013). It also impacts growth and timing of metamorphosis (Larson et al.
57 1998, Allran and Karasov 2000, 2001, Boone and James 2003, Rohr et al. 2004, Forson and
58 Storfer 2006a, Forson and Storfer 2006b).

59 Given considerable interests in the role of physiology to vertebrate survival and
60 conservation (Martin et al. 2010, Rohr et al. 2013b, Madliger et al. 2016), there have been
61 numerous studies on the effects of atrazine on physiology. For example, several studies have
62 investigated atrazine as an ‘infodisruptor’, defined as a chemical contaminant that disrupts
63 communication within or among organisms, including contaminants that breakdown or interfere
64 with detection or production of chemical signals between senders and receivers or those that
65 affect cell-to-cell communication within organisms (e.g. endocrine disruptors)(Lurling and
66 Scheffer 2007, Rohr et al. 2009). Several studies have shown that atrazine can reduce chemical
67 detection of cues from predators and mates (Moore and Waring 1998, Tierney et al. 2007,

68 Ehresam et al. 2016) and others have shown that it can affect cell-to-cell communication by
69 altering hormones, such as stress hormones (Gabor et al. 2016, McMahon et al. 2017), thyroid
70 hormones (Larson et al. 1998), and sex hormones (Hayes et al. 2003, Hayes 2003). Given that
71 much of the controversy regarding atrazine and amphibians involves its effects on amphibian sex
72 hormones and gonadal development, this topic will be discussed in more detail in the “A
73 Timeline of the Atrazine-Amphibian Controversy” section.

74 Interest in chemical contaminants causing non-monotonic dose-responses (those with a
75 change in the direction of the slope) (Welshons et al. 2003, McMahon et al. 2011, Vandenberg et
76 al. 2012, McMahon et al. 2013) has triggered several researchers to examine whether atrazine
77 causes linear or non-linear dose responses. Researchers have detected non-monotonic dose
78 responses on several amphibian hormones, including corticosterone, thyroid hormone, and sex
79 hormones (Larson et al. 1998, Hayes et al. 2003, Hayes 2003, Fan et al. 2007, McMahon et al.
80 2017). Atrazine also regularly has non-monotonic effects on the timing of metamorphosis (Rohr
81 and McCoy 2010b). Although responses on other endpoints have not produced non-monotonic
82 dose responses as regularly, they have regularly produced logarithmic dose responses, where the
83 greatest change in response occurs at low exposure concentrations (Rohr et al. 2004, Rohr et al.
84 2006b, McMahon et al. 2013, Rohr et al. 2013c), supporting the potency of low concentrations of
85 atrazine.

86 Given that many factors have been documented to affect amphibian diseases that have
87 been linked to amphibian declines (Li et al. 2013, Liu et al. 2013, Rohr et al. 2013b, McMahon et
88 al. 2014, Venesky et al. 2014b), interest has grown in the role that atrazine might have on
89 amphibian immunity and infections. Much of this interest accelerated in 2002 after Kiesecker
90 (2002) revealed that atrazine exposure was associated with reduced amphibian immunity and

91 increased trematode infections and the limb malformations they cause. Since then, Rohr and
92 colleagues have found additional support for the immunosuppressive effects of atrazine and
93 increases in trematode infections (Rohr et al. 2008b, Rohr et al. 2008c, Raffel et al. 2009,
94 Schotthoefer et al. 2011, Rohr et al. 2015). Additionally, they showed that atrazine increases
95 exposure to trematodes by reducing phytoplankton, which reduces shading and increases the
96 abundance of periphyton, the food source for snails, which are the intermediate host of
97 trematodes (Rohr et al. 2008c, Raffel et al. 2010, Staley et al. 2010, Staley et al. 2011, Halstead
98 et al. 2014). Atrazine exposure, either alone or in mixtures with other chemicals, has also been
99 associated with reduced immunity and increased amphibian viral, flatworm, and roundworm
100 infections (Gendron et al. 1997, Forson and Storfer 2006a, Forson and Storfer 2006b, Hayes et
101 al. 2006, Kerby and Storfer 2009, Koprivnikar 2010). Recently, atrazine exposure was shown to
102 reduce tolerance of chytrid fungal infections that are associated with worldwide amphibian
103 declines (Rohr et al. 2013c). Tolerance is defined as the ability of hosts to reduce damage
104 caused by parasites (Rohr et al. 2010, Sears et al. 2013, Sears et al. 2015). In a 2010 review
105 (Rohr and McCoy 2010b), atrazine exposure was associated with a reduction in 33 of 43 immune
106 function endpoints and with an increase in 13 of 16 infection endpoints . These numbers were an
107 underestimate (Langerveld et al. 2009) and have increased since this review was published (e.g.
108 Koprivnikar 2010, Rohr et al. 2013c).

109 The documented positive relationship between biodiversity and ecosystem functions and
110 services, such as pest and disease control, primary production, and clean water (Dobson et al.
111 2006, McMahon et al. 2012, Staley et al. 2014, Venesky et al. 2014a, Civitello et al. 2015, Cohen
112 et al. 2016, De Laender et al. 2016) and the importance of indirect effects of chemicals mediated
113 by species interactions (Rohr et al. 2006a, Clements and Rohr 2009, Halstead et al. 2014,

114 Douglas et al. 2015, Staley et al. 2015) has prompted several researchers to study the effects of
115 atrazine on freshwater communities containing amphibians rather than on isolated amphibian
116 species (de Noyelles et al. 1989, Boone and James 2003, Rohr and Crumrine 2005, Rohr et al.
117 2008c, Halstead et al. 2014). Many of these studies report alterations of amphibian growth and
118 abundance that seem to be caused by atrazine-induced changes in photosynthetic organisms. At
119 ecologically relevant concentrations, atrazine is expected to have a bevy of indirect effects by
120 altering the abundance of phytoplankton, macrophytes, (Herman et al. 1986) and photosynthetic
121 and non-photosynthetic organisms in periphyton (Staley et al. 2010, Staley et al. 2011, Staley et
122 al. 2012, Staley et al. 2015), the latter of which is a primary food source for many tadpole
123 species. However, few of the studies focusing on atrazine and freshwater communities
124 containing amphibians distinguish between direct and indirect effects of atrazine.

125 Although atrazine generally does not directly cause amphibian mortality at ecologically
126 relevant concentrations (Solomon et al. 2008, Rohr and McCoy 2010b), there are some studies
127 that suggest that it might increase mortality through indirect effects, such as those described in
128 the infectious disease section above. Others suggest that there might be delayed or persistent
129 effects of atrazine on behavior and physiology that can increase mortality risk (Storrs and
130 Kiesecker 2004, Rohr and Palmer 2005, Rohr and McCoy 2010b, Rohr and Palmer 2013).

131 One of the biggest concerns regarding the effects of atrazine on amphibians is that
132 atrazine regularly interacts with other stressors commonly experienced by amphibians, either
133 additively or synergistically. For example, particular climatic conditions, such as increased
134 drying (Rohr et al. 2004, Rohr and Palmer 2005, 2013) and particular biotic conditions, such as
135 parasitism (Rohr and McCoy 2010b) and predation risk (Rohr and Crumrine 2005, Ehram et al.
136 2016) can be worsened by atrazine. Atrazine also additively or synergistically interacts with

137 other common agrochemicals (Rohr et al. 2008c, Halstead et al. 2014). The exception is that
138 global warming will accelerate amphibian development and thus reduce aquatic exposure to
139 atrazine (Rohr et al. 2011). Clearly, there is a need to understand how climate change will affect
140 exposure and toxicity of atrazine and other chemical contaminants (Rohr et al. 2013a, Landis et
141 al. 2014). Nevertheless, interactions among chemical contaminants or between chemical
142 contaminants and non-chemical stressors are unfortunately rarely considered in most ecological
143 risk assessments of chemicals (Rohr et al. 2016, 2017).

144

145 **Methods**

146 I extracted the data from Figure 5 of Baxter et al. (2011), which include authors who have
147 historically been funded by Syngenta Crop Protection, Inc. In this experiment, various
148 concentrations of atrazine were applied to outdoor mesocosms containing natural algae,
149 zooplankton, and snails, and snail abundance was tracked through time. Given that initial levels
150 of phosphorous and nitrogen could be depleted through time and were not replenished, these
151 essential elements could become limited and cause algal and snail populations to reach carrying
152 capacities or crash. Hence, I calculated the population growth rate of snails in each tank until an
153 apparent carrying capacity or population crash occurred. Thus, growth rates were calculated for
154 the exponential phase of population growth only. The 30 $\mu\text{g/L}$ treatment was excluded because
155 it did not show the same blocking patterns in dissolved oxygen as the other treatments (see
156 Baxter et al. 2011 Table 3, Rohr et al. 2012). I then plotted the population growth rate estimates
157 against log atrazine concentration.

158

159 **Results**

160 Although not reported in the Baxter et al. (2011) paper, there was a clear increase in snail
161 population exponential growth rates as atrazine concentration increased (Fig. 1). These
162 researchers missed this finding in their data because they never calculated population growth
163 rates for the snail populations before they reached a carrying capacity or crashed. These results
164 demonstrate that both Syngenta-funded (Herman et al. 1986, Baxter et al. 2011) and non-
165 Syngenta-funded researchers (Kiesecker 2002, Rohr et al. 2011, Halstead et al. 2017) have
166 demonstrated that ecologically relevant concentrations of atrazine are capable of increasing snail
167 populations, the source of trematode infections to both amphibians and humans. Given the
168 controversy surrounding the effects of atrazine on amphibians, I now follow this reanalysis with
169 a timeline of some of the most salient events in the history of the atrazine-amphibian
170 controversy.

171

172 **A Timeline of the Atrazine-Amphibian Controversy**

173 *The early years*

174 The atrazine-amphibian controversy all began in 1998, when Dr. Tyrone Hayes, a
175 biology professor at the University of California at Berkeley, was hired by EcoRisk Inc., the
176 consulting company that hired several academic scientists to study atrazine on behalf of
177 Syngenta Crop Protection, Inc. The contract covering Dr. Hayes' research, and that of many of
178 the other scientists Syngenta and EcoRisk hired, made clear that Syngenta retained final say over

179 what and whether the scientists could publish. In November of 2000, Hayes quit Syngenta
180 because the company supposedly prevented him from publishing his research showing that levels
181 of atrazine, below the drinking water standard of 3 ppb set by the EPA, caused hermaphroditism
182 and reduced the larynx size of male frogs. According to Hayes, Syngenta and Ecorisk tried to
183 keep him working on atrazine privately, offering him as much as \$2-million in lab support under
184 the auspices of a start-up company owned by his wife. Hayes refused the offer and began
185 replicating the Syngenta-funded studies using independent funds. Soon after breaking ties with
186 EcoRisk and Syngenta, Hayes claims that Syngenta threaten to pull all of UC Berkeley's
187 pharmaceutical and medical funding provided by Syngenta's sister company Novartis Inc. if they
188 tenured Hayes. Despite the ostensible threat, UC Berkeley did eventually tenure Hayes.

189 At a similar time, in the early 2000s, Krista McCoy began a PhD program at the
190 University of Florida in the laboratory of Dr. Tim Gross, a paid EcoRisk consultant. Krista
191 began a mesocosm study examining the effects of atrazine on amphibians. She came in one
192 morning to discover that Gross had ordered the University of Florida's physical facilities to pick
193 up McCoy's mesocosms with a forklift and move them all directly under the roof line of a large
194 nearby building. McCoy was convinced that the mesocosms were moved so they would receive
195 the entire roof's worth of rain, unrealistically diluting the atrazine. McCoy suspended her
196 atrazine work and switched to laboratory of Dr. Louis Guillette, who confirmed McCoy's story.
197 Dr. Gross was eventually let go from the University of Florida.

198 In February of 2002, Dr. Jason Rohr, was hired at the University of Kentucky to study the
199 effects of atrazine on amphibians. In April of 2002, soon after Rohr was hired, Dr. Hayes
200 published his studies repeating the work he originally conducted for Syngenta (Hayes et al.

201 2002b). This work was published in the prestigious *Proceedings of the National Academy of*
202 *Sciences of the United States of the America (PNAS)*, and showed that very low levels of atrazine
203 reduced the larynx size of male frogs and caused male frogs to develop female gonads.
204 According to Hayes, editors at the prestigious journal *Nature* then commissioned him to write a
205 follow-up article on field patterns of atrazine and amphibian gonadal abnormalities that was
206 published in *Nature* in October of 2002 (Hayes et al. 2002a).

207 In November of 2002, attorneys associated with the Center for Regulatory Effectiveness,
208 the Kansas Corn Growers Association, and the Triazine Network (which receive financial
209 support from Syngenta), argued that Hayes' studies did not conform with the 2001 Data Quality
210 Act, which prohibits federal agencies from using scientific findings for which there are no
211 established standards. Their petition successfully blocked the US Environmental Protection
212 Agency (EPA) from considering Hayes' work and atrazine was re-registered for use in October
213 of 2003. Ironically, this was the same month that the European Union banned atrazine because of
214 ubiquitous and unpreventable water contamination (Sass and Colangelo 2006). Because of this
215 petition and the Data Quality Act, the EPA had to revise its Environmental Risk Assessment
216 policies, so that hormone disruption would not be a legitimate reason for restricting the use of a
217 chemical until "appropriate testing protocols have been established." (Sass and Devine 2004).
218 The Data Quality Act has been used widely by industry to block unwanted regulations and as a
219 broader assault on academic freedom (Michaels and Monforton 2005, Rohr and McCoy 2010a).

220 Since leaving EcoRisk and Syngenta in 2000, the relationship between Hayes and
221 Syngenta representatives became further strained. In 2003, Hayes received a job offer from
222 Duke University and made a second visit to the campus. Duke University is close to Syngenta

223 Crop Protection headquarters in Greensboro, North Carolina and to Syngenta's research facility
224 in Research Triangle Park, North Carolina. Once Syngenta found out about the offer, they
225 contacted administrators at Duke. Soon after, Duke University withdrew the offer to Hayes.
226 According to subpoenaed documents revealed in a lawsuit (see below), by interfering with
227 Hayes' job offer, Syngenta was attempting to protect their reputation in their local community
228 and among their employees (Howard 2013a). In October of 2003, The Chronicle of Higher
229 Education published a lengthy article on the damaged relationship between Hayes and Syngenta
230 and the price Hayes had to pay to publish his research (Blumenstyk 2003).

231

232 *Tensions rise*

233 In November of 2003, there was an organized oral session on the effects of atrazine on
234 amphibians at the North American Society for Environmental Toxicology and Chemistry
235 meetings in Austin, TX. In attendance were Hayes, Rohr, several EPA representatives, and
236 Syngenta- and EcoRisk-funded scientists, including Ronald Kendall, the head of the EcoRisk
237 panel coordinating the investigation of atrazine for Syngenta, and Keith Solomon, a long-time
238 Syngenta-funded academic. There was standing room only. Much to the surprise of all, Hayes
239 presented no data. Rather, he presented only emails ostensibly incriminating the EPA and
240 Syngenta associates of colluding to ensure the re-registration of atrazine. Rohr presented his first
241 talk ever on atrazine immediately after Hayes, quite surprised and intimidated by what just
242 transpired. Because of Hayes' bold presentation, SETAC had to hire extra security for their
243 North American Meetings for several years to come. In December of 2004, Hayes continued to
244 keep a target on Syngenta, publishing an article with colleagues in *BioScience* reporting that the

245 single best predictor of whether or not the herbicide atrazine had a significant effect in a study
246 was whether Syngenta funded it (Hayes 2004). That result was highly significant by the usual
247 statistical measures. In 2005, in a lawsuit against the EPA, the Natural Resources Defense
248 Council obtained documents revealing that agency officials met privately with Syngenta more
249 than 40 times while evaluating the toxicity of atrazine (Slater 2012).

250 Hayes and colleagues' assault on Syngenta was getting intense and Syngenta began to
251 even more vigorously fight back. In 2005, Syngenta began spending millions on a Hayes 'smear
252 campaign' where they came up with a long list of methods for discrediting him, such as "have
253 his work audited by 3rd party," "ask journals to retract his science," "set trap to entice him to
254 sue," "investigate funding," and "investigate wife" (Howard 2013a, Aviv 2014). They even
255 bought the worldwide web search results for his name so they could better control what the
256 public read about Hayes and atrazine (Howard 2013a, Aviv 2014). Although Hayes suspected
257 much of this, it was not verified until this smear campaign became public in 2012 when
258 thousands of Syngenta documents were subpoenaed in a lawsuit (Howard 2013a) (see below).

259 Rohr became a bigger target than before in 2008 when he and colleagues published a
260 paper in *Nature* showing that atrazine increased infectious disease risk in a declining amphibian
261 species by reducing frog immunity and increasing its exposure to the pathogen (Rohr et al.
262 2008c). In November of 2008, in response to an accumulation of papers on atrazine and
263 amphibians, Keith Solomon and colleagues, with financial support from Syngenta, published a
264 paper in *Critical Reviews in Toxicology* entitled "Effects of atrazine on fish, amphibians, and
265 aquatic reptiles: a critical review" (Solomon et al. 2008). This paper purported to accurately
266 review the effects of atrazine on the behavior, growth, survival, physiology, endocrinology,

267 gonadal morphology, immunity, and infectious disease risk of amphibians. Rohr, a second year
268 professor at the University of South Florida, eagerly read the review paper but did not recall the
269 primary literature the same way as it was described by Solomon et al. (2008). Around the same
270 time, Krista McCoy, an eventual postdoctoral research associate in Rohr's laboratory, expressed
271 to Rohr that she too did not agree with Solomon et al.'s depiction of the primary literature on
272 atrazine. Hence, Rohr and McCoy collaborated to quantify the inaccurate representations of
273 primary literature in the Syngenta-funded Solomon et al. (2008) article, as well as conduct their
274 own objective meta-analysis of the literature to set the record straight.

275 While Rohr and McCoy worked on their analyses, the heat on atrazine continued to build.
276 In August of 2009, *The New York Times* investigation found that 33 million Americans were
277 exposed to atrazine through drinking water and, later, data from EPA showed that contamination
278 exceeded the federal limit in 9 out of 10 Midwestern states monitoring it. Several of these water
279 districts reported between 9 and 18 times the federal limit, levels linked to birth defects,
280 premature birth, and low birth weight (Slater 2012).

281

282 ***The controversy really escalates in 2010***

283 In January of 2010, Hayes et al. published an elegant experiment in *PNAS* (Hayes et al.
284 2010) where they exposed a laboratory population of all genetically male frogs to low levels of
285 atrazine and showed that these males were both demasculinized (chemically castrated) and
286 completely feminized as adults. Atrazine-exposed genetic males suffered from depressed
287 testosterone, decreased breeding gland size, feminized laryngeal development, suppressed

288 mating behavior, reduced spermatogenesis, and decreased fertility. Additionally, 10% of these
289 males developed into functional females that copulated with unexposed males and produced
290 viable eggs.

291 During the early months of 2010, Rohr and McCoy completed their assessment of the
292 Solomon et al. (2008) article and set the record straight with their own meta-analysis (Rohr and
293 McCoy 2010b). Rohr and McCoy revealed that the Syngenta-funded review by Solomon et al.
294 (2008) had arguably misrepresented over 50 studies and had 122 inaccurate and 22 misleading
295 statements. Of these 144 seemingly inaccurate or misleading statements, 96.5% appeared to be
296 beneficial for Syngenta in that they supported the safety of the chemical (Rohr and McCoy
297 2010a). In addition, Solomon et al. (2008) cast doubts on the validity of 94% of the 63 presented
298 cases where atrazine had adverse effects, whereas they almost never criticized the 70 cases
299 where there were no effects of atrazine at environmentally relevant concentrations (Rohr and
300 McCoy 2010a). Rohr and McCoy then conducted a qualitative meta-analysis on the same data
301 analyzed by Solomon et al. (2008) and the general conclusions were the same regardless of
302 whether they excluded studies based on clear quality criteria or included all studies (Rohr and
303 McCoy 2010b). They showed that atrazine regularly disrupted the timing of amphibian
304 metamorphosis, reduced size at or near metamorphosis, altered amphibian motor activity and
305 antipredator behaviors, reduced olfactory abilities, diminished immune function, increased
306 infection end points, and altered aspects of gonadal morphology and function and sex hormone
307 concentrations, but did not directly affect amphibian survival (Rohr and McCoy 2010b). These
308 two studies were submitted as companion papers to *Environmental Health Perspectives*. The
309 meta-analysis was published there (Rohr and McCoy 2010b) but the editor refused to even
310 review the paper on the conflicts of interest, inaccuracies, and bias of the Solomon et al. (2008)

311 paper. After four additional case where editors did not send the paper out for review in many
312 cases fearing the controversy, Rohr and McCoy put a conservation angle on the conflicts of
313 interest paper and published it in *Conservation Letters* (Rohr and McCoy 2010a). There was
314 surprisingly little push back from Syngenta on these papers. In fact, according to subpoenaed
315 documents, Syngenta representatives prepared their funded scientists on how to respond to
316 difficult questions about these studies, describing the meta-analysis as a “rigorous and
317 comprehensive review”.

318 In July of 2010, Danielle Ivory of the Huffington Post Investigative Fund reported that
319 fewer than 20% of the papers the EPA relied upon in its past decision-making on atrazine were
320 peer-reviewed. Additionally, at least half were conducted by scientists with a financial stake in
321 atrazine (Ivory 2009, 2010). This investigation raised additional concerns over the decision-
322 making process on the safety of atrazine.

323 In August of 2010, Syngenta struck back against Hayes. They released a 102 page PDF
324 file documenting offensive and potentially embarrassing emails sent by Hayes to Syngenta
325 representatives over the years. In these emails, Hayes had used profanities and sexual taunts, and
326 aggressive, salacious, lewd, and insulting language. The NY Times wrote a story about the
327 emails (Schor 2010) and republished the PDF file
328 (http://www.atrazine.com/amphibians/combined_large_pdf-r-opt.pdf). The emails were also
329 covered by *Nature* (Dalton 2010). These emails made it clear that the unprofessionalism and
330 questionable decision making was occurring by both parties. Dashka Slater provided the
331 following quote in her Mother Jones article to describe these emails “His [Hayes] irreverence
332 had always been an asset, attracting attention to atrazine just as Rachel Carson's impassioned

333 lyricism drew attention to DDT. But now irreverence had tipped toward irrationality.” (Slater
334 2012). Based on these emails, Syngenta issued a formal ethics complaint filed at the University
335 of California Berkeley. The university's chief counsel ruled that no ethics violation had occurred
336 but admonished both sides to behave.

337 In 2010, a class-action lawsuit against Syngenta picked up steam. The lawsuit, originally
338 filed in 2004 by Holiday Shores Sanitary District, grew and eventually included more than 1,000
339 community water systems in Illinois, Missouri, Kansas, Indiana, Iowa and Ohio. The lawsuit,
340 led by Stephen Tillery of the law firm Korein Tillery, LLC, was brought because Midwestern
341 water treatment facilities often could not get atrazine concentrations in their drinking water
342 below the US EPA maximum contaminant level deemed safe for human consumption (3 ppb).
343 Rohr passed on testifying in the case (see below), whereas Hayes did testify and Stephen Tillery
344 stated that Hayes’ work gave them the scientific basis for the lawsuit.

345 In 2012, the class-action lawsuit filed in 2004 by Holiday Shores Sanitary District that
346 grew into a class action lawsuit with more than 1,000 community water systems in Illinois,
347 Missouri, Kansas, Indiana, Iowa and Ohio vigorously continued until the integrity of an
348 important witness for Korein Tillery (someone other than Hayes) was questioned after illicit
349 behaviors were allegedly uncovered. Soon after, Tillery and associates settled the suit but
350 Syngenta denied all wrongdoing and did not claim any liability. Syngenta paid \$105 million to
351 reimburse more than a thousand Midwestern water utilities for the cost of filtering atrazine from
352 drinking water. When lawyer fees were removed, this amounted to well under \$100,000 per
353 water treatment plant.

354 Stephen Tillery and another lawyer from his office flew from Illinois to Rohr's office to
355 recruit him as an expert scientist for the case. They offered to pay Rohr generously for his
356 services. Before jumping at the opportunity, Rohr queried Tillery. Rohr asked whether the
357 atrazine problem was not at least partially an issue of how much atrazine was applied in the
358 Midwestern US and that most of the water treatment plants there lacked modern carbon filtration
359 systems necessary to remove the atrazine. Tillery confirmed that this was a major source of the
360 problem. Rohr then made it clear that Syngenta could not control who buys their product, where
361 they apply it, how much they apply, or whether water treatment plants have adequate carbon
362 filtration systems. Hence, Rohr questioned whether the atrazine problem in the Midwestern US
363 was an EPA enforcement issue and whether the EPA, not Syngenta, should be sued. Tillery
364 agreed with all the logic but claimed that he could not sue the EPA. Rohr, however, made it
365 clear to Tillery that he could sue the EPA because the Natural Resource Defense Council sues
366 the EPA all the time; law firms just cannot sue the EPA for money. Rohr politely declined the
367 offer to be an expert witness, worried that the lawsuit was misdirected at the entity with the
368 deepest pockets.

369 In November of 2010, Rohr gave a seminar on atrazine at Illinois State University the
370 year after Hayes gave his seminar there. Illinois State University is not far from Syngenta's US
371 headquarters in Illinois. In preparation for the seminar, Illinois State University's Department of
372 Biology hired a security guard to staff the talk. Syngenta sent an attorney in a three piece suit
373 that was frisked by the security guard to check for recording devices. The attorney took copious
374 notes throughout the talk.

375 After the flurry of papers published by Rohr’s laboratory between 2008 and the
376 beginning of 2011 on atrazine and chlorothalonil, two pesticides produced by Syngenta, Rohr
377 started receiving pushback from the Director of the facility where Rohr conducted his outdoor
378 tank (mesocosm) experiments on agrochemicals. Rohr collaborated with Dr. Steven Johnson of
379 the University of Florida’s Gulf Coast Research and Education Center (GCREC), which was just
380 45 minutes from the University of South Florida where Rohr is employed. This collaboration
381 allowed Rohr to have his tank facility at GCREC. The Director of the GCREC’s wife worked
382 for Syngenta at the time. Rohr and Johnson did not face any challenges until they started
383 publishing their findings. Johnson surprisingly found out that he was being forced out of the
384 GCREC back to the main campus of the University of Florida in Gainesville. Given that
385 Johnson was no longer at the GCREC, the Director of the GCREC told Rohr he also had to leave
386 because his collaborator was no longer at the facility. Rohr resourcefully looked to find another
387 collaborator at the GCREC so he could continue his work there. He found two faculty members
388 other than Johnson that wanted to collaborate but the Director of the GCREC blocked both
389 collaborations and eventually told all GCREC faculty that they could not collaborate with Rohr
390 or conduct any pesticide-related toxicological research, stifling their academic freedoms. It took
391 Rohr several years to find a location and setup another tank facility, a major impediment to his
392 ecotoxicological research on atrazine and other agrochemicals.

393

394 ***Revelations from the lawsuit and the EPA scientific advisory panel***

395 The most important outcome of the lawsuit was not the settlement but the Syngenta
396 documents that became “unsealed” by the Madison County Circuit Court in response to a

397 Freedom of Information Act request by the courageous investigative reporting conducted by
398 Clare Howard of 100Reporters. The 1,000 or so pages of memos, notes, and e-mails that Clare
399 received exposed Syngenta's tactics and efforts to conceal and discredit the science on atrazine.
400 They revealed that Hayes was not paranoid after all and that Syngenta was indeed behind a
401 campaign to smear him and his reputation. The subpoenaed documents revealed that one of the
402 company's strategies had been to *"purchase 'Tyrone Hayes' as a search word on the internet, so*
403 *that any time someone searches for Tyrone's material, the first thing they see is our material."*
404 Syngenta later also purchased the phrases "amphibian hayes," "atrazine frogs," and "frog
405 feminization" and searching online for "Tyrone Hayes" for years until the settlement brought up
406 an advertisement that said, "Tyrone Hayes Not Credible." The documents revealed that
407 Syngenta invested in a multi-million dollar campaign to protect atrazine profits, which included
408 hiring a detective agency to investigate scientists on a federal advisory panel, looking into the
409 personal life of a judge, and discrediting and distracting Hayes. These documents also listed
410 other strategies directed at Hayes, such as *"commissioning a psychological profile"*, *"have his*
411 *work audited by 3rd party"*, *"ask journals to retract"*, *"set trap to entice him to sue"*. *"investigate*
412 *funding"*, *"investigate wife"*, *"tracking him at speaking engagements"*, *"baiting him through*
413 *emails"*, and interfering with Hayes' job offer at Duke. Syngenta would send representative to
414 talks Hayes gave to question and embarrass him. Rohr too had similar experiences. The
415 documents also revealed that Syngenta kept a list of 130 people and groups it could recruit as
416 experts, including academics, without disclosing ties to the company (see
417 [https://www.documentcloud.org/documents/686401-100reporters-syngenta-clare-howard-](https://www.documentcloud.org/documents/686401-100reporters-syngenta-clare-howard-investigation.html)
418 [investigation.html](https://www.documentcloud.org/documents/686401-100reporters-syngenta-clare-howard-investigation.html) for the list). It often paid members of this group to write opeds and other
419 articles. According to Jayne Thompson from Jayne Thompson & Associates, a public relations

420 firm hired to work on the Syngenta campaign, “*These are great clips for us because they get out*
421 *some of our messages from someone who comes off sounding like an unbiased expert. Another*
422 *strength is that the messages do not sound like they came from Syngenta.*” Clare Howard
423 summarizes her investigative reporting on these documents in a ground breaking article
424 published in June of 2013 in a 100Reporters (Howard 2013a). Unfortunately, these documents
425 did not get considerable press until February of 2014 when the more well-known magazine *The*
426 *New Yorker* released an article on atrazine, Hayes, and the uncovered Syngenta documents (Aviv
427 2014). The original *New Yorker* article inexplicably did not acknowledge any of Clare’s seminal
428 investigative work (Aviv 2014).

429 Ironically, as the class-action lawsuit was being settled, so too were the policy decisions
430 on the safety of atrazine to amphibians. The EPA had convened a scientific advisory panel to
431 assess the effects of atrazine on amphibians and originally offered Rohr to be a member on this
432 panel. The EPA then rescinded this offer because Rohr’s work would serve too prominently in
433 panel discussions. The EPA then recruited Dr. Michelle Boone to take Rohr’s place. The
434 USEPA concluded that “*exposure to atrazine at concentrations ranging from 0.01 to 100*
435 *[milligrams per liter] had no effect on Xenopus laevis [an amphibian species] development*
436 *(which included survival, growth, metamorphosis, and sexual development)*” (p. 60) and that the
437 “*level of concern for effects on aquatic plant communities... was lower than the atrazine*
438 *concentration observed to produce significant direct or indirect effects on invertebrates, fish,*
439 *and amphibians*” (USEPA 2012), which would eliminate further assessments of atrazine’s
440 impacts on amphibians despite significant effects at these concentrations in other studies. The
441 EPA’s conclusion that atrazine does not adversely affect amphibians, however, was based on a
442 single published study that was funded by Syngenta, despite there being hundreds of studies on

443 atrazine. Several members of the scientific advisory panel argued that a decision on the safety of
444 atrazine should not be made based on any single study, especially one funded by the company
445 with a financial stake in the product. In fact, after finishing her work on the scientific advisory
446 panel, Boone collaborated with Rohr and other colleagues to write articles denouncing the use of
447 a single industry-funded study to evaluate the adverse effects of atrazine, or for that matter, any
448 chemical (Boone et al. 2014, Boone and Rohr 2015).

449 In April of 2014, Rohr, Hayes, and Solomon appeared on 16x9, a Canadian National
450 Television primetime news show similar to 60 Minutes, 20/20, or Dateline in the US
451 (<http://globalnews.ca/video/1252483/full-story-pesticide-peril>). The story was produced by Gil
452 Shochat and summarizes the story of the amphibian-atrazine controversy. It also offers an
453 interview with a former Syngenta staffer who describes Syngenta's internal strategies for
454 discrediting scientists.

455

456 *Three additional surprising twists*

457 In August of 2014, UC Berkeley shut down Hayes' amphibian research because Hayes
458 did not have sufficient funds to pay for his vertebrate animal care. Hayes claimed that his lab
459 fees had gone up by 295% since 2004, while fees for his colleagues at UC Berkeley had risen by
460 only 15% (Howard 2013b). The director of the office of laboratory-animal care apparently
461 provided evidence that Hayes was being charged according to standard campus-wide rates that
462 increased for most researchers in recent years. Nevertheless, Hayes recruited Stephen Tillery to

463 represent him in a lawsuit against UC Berkeley claiming that his vertebrate animal care fees
464 were essentially preventing him from doing his job. The status of this case is currently unclear.

465 In 2016, after the damaging press of the unsealed court documents, Syngenta announced
466 that it was set to be acquired by Chinese state-owned ChemChina (Spegele and Chu 2016).
467 However, Syngenta and ChemChina missed the European Union’s deadline for submission of
468 antitrust remedies (Blackstone and Drozdiak 2016), raising questions regarding whether they will
469 be able to satisfactorily deal with the antitrust concerns. It remains unclear whether the deal will
470 happen and if the tactics of Syngenta will change if the sale occurs.

471 In May 2007, the Center for Biological Diversity filed a lawsuit against the EPA for
472 violating the Endangered Species Act by registering and allowing the use of many pesticides
473 without determining whether the chemicals jeopardized endangered species in the San Francisco
474 Bay. A federal court then signed an injunction, imposing interim restrictions on the use of 75
475 pesticides in the Bay Area. This in turn required that the EPA formally evaluate the effects of
476 those chemicals on endangered species. In June of 2015, the EPA announced that it would
477 analyze the effects of glyphosate (active ingredient in the herbicide Roundup) and atrazine on
478 1,500 endangered plants and animals (Beyond_Pesticides 2015). Likely as a result of this court
479 order, the EPA re-evaluated atrazine and, apparently in error, released the report online in April
480 of 2016, a presidential election year. This sparked criticism from Syngenta and U.S. lawmakers
481 (Polansek 2016).

482 In perhaps the most surprising twist of all, the EPA completely reversed its position on
483 the safety of atrazine in this “inadvertently” released reassessment of atrazine. Despite the EPA
484 concluding that atrazine was safe for over four decades, the new and refined risk assessment

485 (Farruggia et al. 2016) states the following: “*Based on the results from hundreds of toxicity*
486 *studies on the effects of atrazine on plants and animals, over 20 years of surface water*
487 *monitoring data, and higher tier aquatic exposure models, this risk assessment concludes that*
488 *aquatic plant communities are impacted in many areas where atrazine use is heaviest, and there*
489 *is potential chronic risk to fish, amphibians, and aquatic invertebrates in these same locations.*
490 *In the terrestrial environment, there are risk concerns for mammals, birds, reptiles, plants and*
491 *plant communities across the country for many of the atrazine uses. EPA levels of concern for*
492 *chronic risk are exceeded by as much as 22, 198, and 62 times for birds, mammals, and fish,*
493 *respectively. For aquatic phase amphibians, a weight of evidence analysis concluded there is*
494 *potential for chronic risks to amphibians based on multiple effects endpoint concentrations*
495 *compared to measured and predicted surface water concentrations... average atrazine*
496 *concentrations in water at or above 5 µg/L for several weeks are predicted to lead to*
497 *reproductive effects in fish, while a 60-day average of 3.4 µg/L has a high probability of*
498 *impacting aquatic plant community primary productivity, structure and function.” It remains*
499 unclear why the EPA changed its opinion on the safety of atrazine, how the report was
500 “inadvertently released”, and what its consequences will be. However, if there is one thing that I
501 have learned about the science and policy decisions on atrazine, it is to expect the unexpected!

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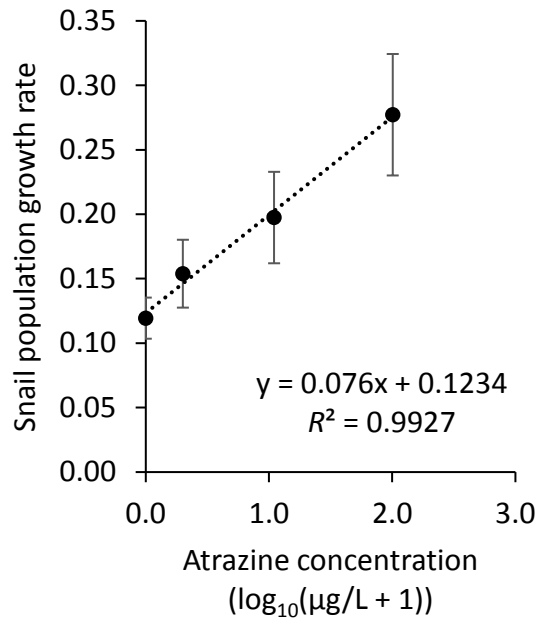
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788 **Fig. 1.** The population growth rate of snails in outdoor mesocosms containing 0, 1, 10, 100 µg/L
789 of atrazine in the Syngenta-funded study by Baxter et al. (2011). Growth rates are calculated for
790 the exponential phase until a carrying capacity or decline in growth occurred. The 30 µg/L
791 treatment was excluded because it did not show the same spatial blocking patterns in dissolved
792 oxygen as the other treatments (see Rohr et al. 2012).