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# Corrigendum

# Second Generation of Antisense Oligonucleotides: From Nuclease Resistance to Biological Efficacy in Animals

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In April 1996, we published an article on the second generation of antisense oligonucleotides (*H.E. Moser et al., Chimia* **1996**, *50*(4), 168–176). One year ago, we discovered that a single individual scientist in the *Novartis* Research Department in Basel, Switzerland, was responsible for several cases of experimental data manipulation. This individual confessed to data manipulation which affected tumor xenograft results obtained with some of our antisense inhibitors. Two of the figures (*Fig. 8* and *9*) from our *CHIMIA* publication were generated under the supervision of this individual and, as such, have affected the validity of some of the results described therein. Since the discovery of this incident, *Novartis* and *Isis* have jointly and aggressively worked hard to determine which experiments were affected and to repeat the key experiments as necessary. Our analysis of the data contained within the *CHIMIA* report is complete and I want to now inform you of our conclusions regarding this issue.

Based on a detailed review of all data pertaining to C-raf and PKC-$\alpha$ antisense compounds in cell culture (*in vitro*) and animal (*in vivo*) models, we have performed an extensive re-evaluation of CGP-69846/ISIS 5132 in tumor xenograft models. These studies were conducted at *Isis*, *Novartis*, and with outside research collaborators. Our conclusions resulting from this review and re-evaluation are summarized as follows:

1. All of the chemical, biophysical, cell culture, pharmacokinetic, toxicologic, and conceptual statements are accurate (*Fig. 1–7, 10, 11*).
2. C-raf and PKC-$\alpha$ antisense molecules each display significant *in vivo* antitumor activity against a number of tumor types in xenograft models including U87 glioblastoma (C-raf/PKC-$\alpha$), SQ-20B laryngeal carcinoma (C-raf), Calu-1 lung carcinoma (C-raf/PKC-$\alpha$), and MDA-MB-231 breast carcinoma (PKC-$\alpha$). *In vivo* activity of 2$^{nd}$-generation molecules is significantly greater than that of 1$^{st}$-Generation antisense molecules targeted against C-raf and PKC-$\alpha$.
3. The doses required to observe antitumor activity in these models are generally higher than those which were reported (10–20 mg/kg *vs.* 0.6 mg/kg).
4. C-raf and PKC-$\alpha$ antisense molecules do not display significant antitumor activity against the tumor type (A549 lung carcinoma) described in the report at doses less than or equal to 25 mg/kg.

We deeply regret any problems that this incident may have caused to *CHIMIA* and to the scientific community at large.

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