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December 22, 2008

Federal Trade Commission
Office of the Secretary
Room H-135 (Annex F)
600 Pennsylvania Avenue, NW
Washington, DC 20580

RE: "Emerging Health Care Competition and Consumer Issues – Comment, Project No. P08390"

Dear Commissioners:

Thank you for the opportunity to submit comments related to the recently held FTC Roundtable on the Emerging Healthcare Competition and Consumer Issues. I thank you for the opportunity to participate in the Roundtable and offer these comments to address some of the questions that were raised during the Roundtable. Brill (2008) explores the question of data exclusivity for follow-on biologic drugs and concludes that seven years of data exclusivity will appropriately balance benefits of innovation and competition. These comments elaborate on the research presented in that paper.

My four key points can be summarized as follows:

1. Brill (2008) extends a "break-even analysis" model first proposed by Henry Grabowski (Grabowski 2008) to incorporate innovator firm profits post-exclusivity and adjusts other factors to more plausible assumptions. The conclusion of Brill (2008) is that a data exclusivity period of seven years would result in an appropriate balance between innovation and competition.
2. Results presented in Brill (2008) contain conservative assumptions, likely to under-estimate the expected profits for innovator drugs following introduction of follow-on biologic drugs. Specifically, prices for an innovator drug are likely to decline less than assumed in the model, and perhaps not at all. In addition, the assumption regarding the timing for a follow-on biologic drug to enter the market is likely underestimated. More moderate assumptions for these variables would result in modestly higher expected profits for the innovator drug and a slightly shorter break-even point. However, a balanced policy recommendation remains seven years of data exclusivity.
3. Data exclusivity is important for encouraging research and innovation for new biologic drugs. In addition, policymakers should consider properly designed incentives for encouraging post-market innovation. However, simply imposing a long initial data exclusivity period is neither an efficient, nor appropriate tool for this goal.
4. Lastly, I report the model underlying results in Brill (2008). In addition, I present an alternative interpretation of sales-weighted market share from Brill (2008). However,

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for modest price decline assumptions, the change in the break-even point is very small. Important empirical assumptions in Brill (2008) rely on the Congressional Budget Office estimate of S. 1695, though as discussed below, their estimates can lead towards overly conservative parameters. Finally, to demonstrate the sensitivity of the model to a range of plausible assumptions, I present break-even results for alternative assumptions.

Below I address each of the above points in greater detail.

Break-even analysis is one useful tool for exploring the effects of data exclusivity on incentives for research and development of innovative drugs.

Employing data on historical R&D costs, probabilities of clinical trial success, and drug sales; and estimates of post-approval R&D, marginal production costs (e.g. contribution margin) and cost of capital, Grabowski (2008) outlines and implements a model to estimate the expected "break-even point" for a portfolio biologic investment. Brill (2008) modifies Grabowski's model by employing two alternative assumptions, and extends the model for the purpose of analyzing the impact of data exclusivity and competition from follow-on biologics on the economic profits post-exclusivity.

This modeling strategy is a well-established tool of financial analysis and is probably the best mechanism to provide empirical estimates of the dynamics of the biologics market, and thus model investment decisions. Nevertheless, both Grabowski (2008) and Brill (2008) rely on a plethora of data and assumptions and a degree of uncertainty exists for either estimate. As demonstrated below, a sensitivity analysis to some assumptions in Brill (2008) suggests a slight variation in results, but no fundamental change in the break-even point.

In addition, it is important to acknowledge that there exist additional considerations that are not modeled. Legislative and regulatory considerations beyond the question of data exclusivity will affect the ability of follow-on biologics to enter the marketplace. First, regulations defining the pathway for approval of a follow-on biologic, and second, patents, including resolution of patent disputes would affect the timing of entry for biogeneric drugs. Third, factors such as "evergreening" of an innovator product could prevent entry by competing biogenerics.

Brill (2008) contains conservative assumptions, potentially under-estimating the expected profits for innovator drugs following introduction of follow-on biologic drugs.

The Brill model of post-data exclusivity profits for an innovator firm uses estimates derived from a Congressional Budget Office cost estimate for "S. 1695, Biologics Price Competition and Innovation Act of 2007" (CBO 2008) to inform the assumptions regarding the effects of competition on the biologics market. Three key estimates from CBO (2008) enter the model directly (price effects, expected delay for entry of FOBs and sales weighted market-share). In addition, Brill (2008) assumes, conservatively, no change in total market sales following entry of follow-on biologic drugs to the market.

Price decline assumption

The CBO estimate of S. 1695 reports the following:

> *"With respect to price discounts, CBO estimates that during the first year of competition, the sales-weighted market average discount on FOBs relative to brand-name innovator drugs would be about 20 percent, reaching 25 percent in the most competitive markets. By the fourth year of competition, we anticipate that the sales-weighted average discount of the FOB relative to the brand-name price would reach about 40 percent. We expect that the availability of FOBs would constrain brand-name prices,"* (p. 7).

Put directly, CBO estimates FOB prices will be 40 percent lower than the innovator drug price and that FOBs would "constrain" innovator prices, but no specific detail in that assumption is revealed. Because it is the innovator price that matters, not the FOB price, there is an inherent insufficiency in the CBO analysis for our purposes.

Given the desire to impose conservative assumptions, the Brill model assumes the price decline of innovator drugs is equal the FOB price. In fact, this is an extreme assumption given that CBO clearly indicates that there will be a price difference between the FOB and innovator product.

Time for regulatory approval for FOB drug

The Brill model assumes that FOB entry occurs one year after the end of the data exclusivity period. This assumption appears conservative given the time involved in developing a FOB, the expected regulatory hurdles from FDA for clinical data and a time for regulatory review. CBO (2008) implies a two year delay from the time at which the first follow-on biologic drugs could legally enter the market and when competition for most products would begin to occur (p. 6). In addition, Ahlstrom, et. al. (2007) in a paper on potential cost savings from FOB entry, assumes a 2-year period for FDA review for approval of a FOB. Any delay in competition beyond the one year assumed in Brill (2008) would result in additional profits for the innovator drug post-exclusivity.

Total market size assumption

The CBO score reveals little about their assumption for the total market size, post-exclusivity when they state:

> *"[B]ecause a FOB would be less expensive than the original innovator product, we expect that demand for such therapies would increase, thus offsetting a small portion of the savings generated by the switching of patients who would have used the original innovator product (or a therapeutic alternative) to the competing FOB version,"* (p. 7).

The total market for biologic drugs will grow as a result of FOB entry. Thus the market-share held by the innovator drug industry (65%) would draw from a larger market than in the case of no competition. Because CBO does not specify the expected

increase in total market sales, Brill (2008) makes the assumption that total sales are constant.

Policymakers should consider properly designed incentives for post-approval innovation.

Calfee (2008) and Grabowski (2008) both argue the importance of post-approval research for new drug indications for biologic drugs. Incentives for undertaking post-approval research are an important policy concern. However, there are two important observations regarding design principles for such a policy. First, it should be incremental in nature in order to provide an incentive only to those who innovate. Second, depending on design, a post-approval research incentive could reduce the duration of the initial data exclusivity period. A long data exclusivity period for the initial approval is not an efficient policy for encouraging post-approval research.

Sensitivity Analysis to Brill (2008)

I next explore the effects of alternative price decline assumptions and an alternative interpretation of sales-weighted market share.

According to the CBO cost estimate of S. 1695:

> *"CBO expects that during the first year of FOB competition, the market share of a FOB would be about 10 percent. By the fourth year, we estimate that the sales-weighted average market share would increase to about 35 percent,"* (p. 7).

From this statement, I geometrically extrapolated the change in sales-weighted market share in the second and third years, and assumed no change in sales-weighted market share after the fourth year.

I interpreted this estimate as follows: The percent market share of the follow-on biologic adjusted for sales is measured as the price of the follow-on biologic multiplied by the quantity of the drug sold. Notably, the "sales-weighted" term in the definition distinguishes this interpretation for simple "market share" measured in terms of quantity sold taken alone. A useful illustration of the difference between these two measures can be drawn from a stylized example of the car market.

> Example. Assume there are two types of cars in South Beach, Florida: Ferraris and Toyotas. Ferraris cost $80,000 and Toyotas cost $20,000. Assume also that there are 10 cars sold this year: 7 Ferrari and 3 Toyotas. Whereas the market share in terms of quantity for Toyota is 30% (three out of ten), the market share weighted for sales would be approximately 10% ($60,000 out of $620,000).

Because sales data – average price multiplied by volume – is the most readily available data for biologic drug companies and average price and units is not generally reported on a consistent basis by companies, this is the logical interpretation of the CBO estimate. Furthermore, the Grabowski (2008) model is constructed based on total sales data as an initial input to the model, not price and volume estimates separately. The appendix, where underlying model is fully described includes the mathematical

intuition of both interpretations of sales weighted market share. Importantly, if the price decline for the innovator drug is small (or zero) the empirical impact is near zero (or zero).

The following illustration shows break-even analysis for a representative portfolio of biologic drugs with a ten percent discount rate and sixty-percent contribution margin. The lines represent alternative assumptions regarding price decline and the effect of varying the interpretation of sales-weighted market share. The top line represents the break-even point and expected economic profits without any FOB competition. The four lower lines all assume seven years of data exclusivity but vary assumptions about price effect and the interpretation of sales-weighted market share. The bottom line represents the alternative interpretation of sales-weighted market share and assumes that innovator prices decline to match the FOB price, namely 10 percent in the first year growing to 40 percent in the fourth year. The dotted line represents the results previously presented in Brill (2008). It differs from the lower line only in the interpretation of sales-weighted market share. The line with square markers assumes that innovator drug prices decline only 5 percent in the first year reach 20 percent in the fourth year and the assumes the alternative interpretation of sales-weighted market share (K'). Finally, the light blue line with the hash marks represents profits if innovator drug prices do not fall at all and innovators drugs only lose market share. In this case, the interpretation of sales-weighted market share does not matter.

A few observations: First, in all cases (assuming seven years of data exclusivity), the portfolio breaks-even and generates economic profits for investors (e.g. profits exceed of the required rate of return). Second, in all three cases, the portfolio breaks even before 14 years and generally in 9 or 10 years. Third, it is important to acknowledge a degree of uncertainty in the expected profits for this portfolio investment. Nevertheless, across a range of alternative assumptions seven years of data exclusivity will allow investors to "break-even" and earn economic profits.

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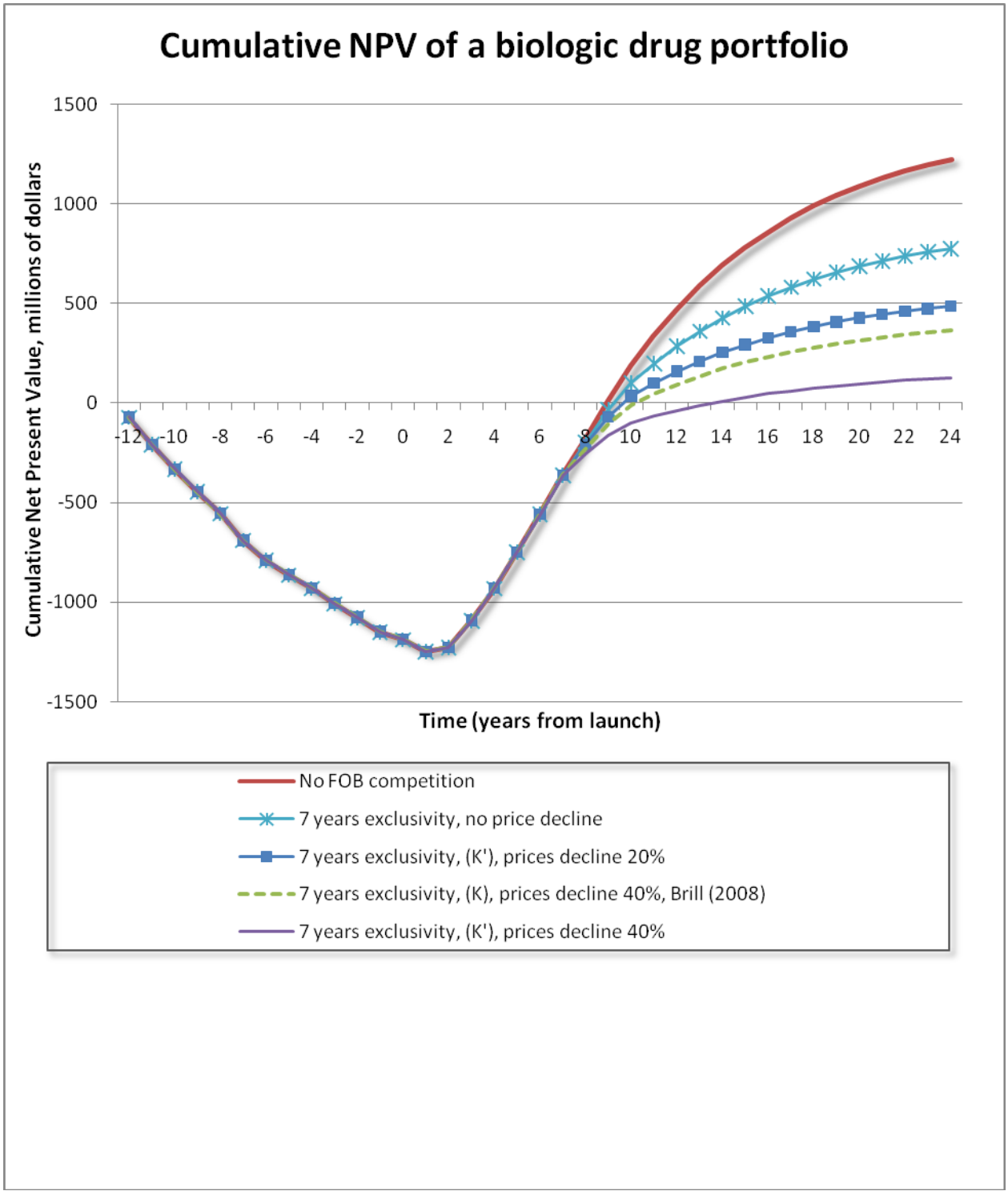

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Brill (2008)

Using the Congressional Budget Office estimates reported for S. 1695 (CBO 2008) and those reported in Grabowski (2008), the following model for post-data exclusivity profits for the innovator drug company was derived. First, I summarize the estimates for pre-data exclusivity expiration firm profits:

T0 = Pre-data exclusivity expiration

V_{f0} = *Volume in T0*

P_{f0} = *Price in T0*

C_{f0} = *Cost of Production in T0*

X_{f0} = *Profit in T0*

S_{f0} = *Sales in T0* = $V_{f0} * P_{f0}$

CM_0 = *Contribution Margin in T0, where Contribution Margin* = $(P - C)/P$

Grabowski's paper offers estimates of sales ($S_{f0} = V_{f0} * P_{f0}$) and the contribution margin ($CM_0 = (P - C)/P$) but does not reveal assumptions about volume (V), price (P) or cost of production (C). We assume that in T0, all firm-level estimates are also true for the market as a whole, since the market has been protected from competition by the data exclusivity provision.

The profit of the firm in T0 is equal to the volume of the drug sold multiplied by the difference between the price of the drug and the cost of producing the drug.

$$X_{f0} = V_{f0} * (P_{f0} - C_{f0})$$

And therefore:

$$X_{f0} = (P_{f0} * V_{f0}) * ((P_{f0} - C_{f0})/P_{f0})$$

$$X_{f0} = (P_{f0} * V_{f0}) * CM_0$$

For the market as a whole,

$$X_{m0} = V_{m0} * (P_{m0} - C_{m0})$$

$$X_{m0} = (P_{m0} * V_{m0}) * ((P_{m0} - C_{m0}) / P_{m0})$$

$$X_{m0} = (P_{m0} * V_{m0}) * CM_0$$

Next, I explore what would happen after competition enters the market.

Post-data exclusivity expiration = T1

D = *Price decline for innovator drug price*

K = *Sales-weighted market share decline* = $1 - ((P_{f1} * V_{f1}) /(P_{m1} * V_{m1}))$

[or, $((P_{f1} * V_{f1}) /(P_{m1} * V_{m1})) = (1 - K) * ((P_{f0} * V_{f0}) / (P_{m0} * V_{m0}))$

$((P_{f1} * V_{f1}) / (P_{m1} * V_{m1})) / (1 - K) = ((P_{f0} * V_{f0}) / (P_{m0} * V_{m0})) = 1$]

V_{m1} = *Market Volume in T1*

P_{m1} = *Market Price in T1*

X_{m1} = *Market Profit in T1*

S_{m1} = *Market Sales in T1*

V_{f1} = *Firm Volume in T1*
P_{f1} = *Firm Price in T1* = $P_{f0} * (1 - D)$
C_{f1} = *Firm Cost of Production in T1*
X_{f1} = *Firm Profit in T1*
S_{f1} = *Firm Sales in T1*

I assume that the cost of producing the drug does not change from T0 to T1, and that the costs of production are the same for the innovator drug and the follow-on biologic ($C_{f0} = C_{f1} = C_{m1}$). I assume, conservatively, that the total sales for the market in T0 is equal to total sales in T1 ($S_{f0} = S_{m0} = S_{m1}$). To determine profits for the innovator drug market after market competition from FOBs, I first need to determine the contribution margin for innovator drugs in T1:

$$CM_0 = (P_{f0} - C_{f0}) / P_{f0}$$
$$CM_0 * P_{f0} = P_{f0} - C_{f0}$$
$$C_{f0} = P_{f0} - CM_0 * P_{f0}$$
$$C_{f0} = (1 - CM_0) * P_{f0}$$

$$CM_1 = (P_{f1} - C_{f1}) / P_{f1}$$
$$CM_1 = (P_{f0} * (1 - D) - C_{f1}) / (P_{f0} * (1 - D))$$
$$C_{f1} = P_{f0} * (1 - D) * (1 - CM_1)$$

$$P_{f0} * (1 - CM_0) = P_{f0} * (1 - CM_1) * (1 - D)$$
$$(1 - CM_0) / (1 - D) = 1 - CM_1$$
$$CM_1 = 1 - ((1 - CM_0) / (1 - D))$$
$$CM_1 = (1 - D) / (1 - D) - ((1 - CM_0) / (1 - D))$$
$$CM_1 = ((1 - D) - (1 - CM_0)) / (1 - D)$$
And therefore
$$CM_1 = (CM_0 - D) / (1 - D)$$

Now, I can model the change in profits after the data exclusivity period ends:

In T1:

$$X_{f1} = V_{f1} * (P_{f1} - C_{f1})$$
$$X_{f1} = (P_{f1} * V_{f1}) * ((P_{f1} - C_{f1})/P_{f1})$$
$$X_{f1} = (P_{f1} * V_{f1}) * CM_1$$
$$X_{f1} = (P_{m1} * V_{m1}) * ((P_{f1} * V_{f1}) / (P_{m1} * V_{m1})) * CM_1$$
$$X_{f1} = (P_{m1} * V_{m1}) * ((P_{f0} * V_{f0}) / (P_{m0} * V_{m0})) * (1 - K) * CM_1$$
$$X_{f1} = S_{m1} * ((P_{f0} * V_{f0}) / S_{m0}) * (1 - K) * CM_1$$
$$(S_{m1} = S_{m0})$$

And therefore

$X_{f1} = P_{f0} * V_{f0} * (1 – K) * ((CM_0 - D) / (1 – D))$

Alternative interpretation of K

If one were to adopt an alternative interpretation of sales-weighted market share decline to mean solely a decline in the quantity of goods sold, rather than the quantity multiplied by the price, a slightly different result is derived. This model requires assuming that the total volume of the drug sold does not change after competition enters the market.

Next I explore the effect of this alternative interpretation for sales-weighted market share decline, which I will denote K', instead of K.

K' = sales-weighted market share decline is only a change in quantity

$(V_{f1} / V_{m1}) = (V_{f0} / V_{m0}) * (1 - K')$

$(V_{f1} / V_{m1}) = (V_{f0} / V_{m1}) * (1 - K')$

$V_{f1} = V_{f0} * (1 - K')$

$(V_{f1} / V_{m1}) / (1 - K') = (V_{f0} / V_{m0}) = 1$

Then, in T1:

$X'_{f1} = (P_{f1} * V_{f1}) * CM_1$

$X'_{f1} = P_{f0} * (1 – D) * V_{f1} * CM_1$

$X'_{f1} = P_{f0} * (1 – D) * V_{f0} * (1 – K') * CM_1$

Recalling that $CM_1 = (CM_0 - D) / (1 - D)$, the post-data exclusivity profit (X_{f1}) is:

$X_{f1} = P_{f0} * V_{f0} * (CM_0 - D) / (1 - D)* (1 – K)$,

The alternative interpretation, K', yields post-data exclusivity profit (X'_{f1}):

$X'_{f1} = P_{f0} * V_{f0} * (CM_0 - D)* (1 – K')$

The resulting difference between X'_{f1} and X_{f1} is the term (1 – D). For large values of D (D always <1), profits for the innovator will be lower assuming K'. If D=0, $X_{f1} = X'_{f1}$.

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References

Ahlstrom, A., et. al. (2007) Modeling Federal Cost Savings from Follow-On Biologics. Avalere Health. [http://www.avalerehealth.net/research/docs/Modeling_Budgetary_Impact_of_FOBs.pdf]

Brill, A.M. (2008) Proper Duration of Data Exclusivity for Generic Biologics: A Critique. Matrix Global Advisors, LLC, White Paper**.** [http://www.tevadc.com/Brill_Exclusivity_in_Biogenerics.pdf]

Calfee, J., (2008) When Patents Are Not Enough: Data Exclusivity for Follow-On Biologics. American Enterprise Institute, Health Policy Outlook No.10, December. [http://www.aei.org/docLib/20081208_23731HPO10Calfee_g.pdf]

Congressional Budget Office (2008) S. 1695: Biologics Price Competition and Innovation Act of 2007. Congressional Budget Office Cost Estimate. June 25. [http://www.cbo.gov/ftpdocs/94xx/doc9496/s1695.pdf]

Grabowski, H. G. (2008) Follow-on biologics: data exclusivity and the balance between innovation and competition. *Nature Reviews Drug Discovery*. Advance Online Publication, 12 May. [http://fds.duke.edu/db?attachment-25--1301-view-503]

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