[illegible] & Herer, Th let March 18th/80

Re your CH:RY, File: K-134-2) advising me of the rejection of my ~~patent~~ application & the reasons for this -

Japanese patent No 26463/78

~~I would point out how that~~ yr patent office does not seem to realise the significance of my discovery.

Until ~~I read my paper~~ the short abstract of my paper appeared in the programme of the 9th Int Cong of Chemotherapy & became available to delegates to the Cong on July 13 1975 & when I read the full paper on July 15th 1975 at the Congress ~~on~~ no one had ever suggested that RA was due to a protozoal infect and no scientific papers had ever been published suggesting this - I myself, for various reasons ~~wh were never published~~, had considered for some yrs the likelihood that RA could well be of protozoal origin ~~for some years~~ though I had never publ- any articles suggesting this.

Furthermore Clot- ~~was used as an ant~~ which had not yet been used commercially ~~as an~~ at the time of my first experiments

with this drug, which had been developed by the makers (Bayer) as an anti fungal agent & they were not aware that it might have an anti-protozoal effect. Except against Histoplasma as recorded in their investigations reported

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issued in 1974. Even after the reading of my paper on July 15 1975 they still maintained that it had no general anti protozoal effect. However in unpublished work at that time I had shown in the laboratory that a fraction of amoeba of the genus Naegleria could be recovered from all the tissues in cases of acute RA & that in this laboratory this was inhibited or killed by Clot. Because of these findings it seemed reasonable to try the effect of Clot on cases of acute RA & I reported my results to the 9th Int Congress of Chemotherapy paper being read on July 15/75. The findings in my paper concluded the suggestion that RA must be due to a protozoal infection. This was the first suggestion

ther put forward of the protozoal nature of the disease - The reading of my paper must have been taped since ~~by~~ much of it was reported by A.P. & appeared in newspapers & seminals all over the world, ~~although~~ ~~# by actual~~ the reports of my remarks were inaccurate ~~Here~~ This accounts for the articles 1, 2, 3 & 4.

Having discovered the beneficial effects of Clet- in RA cases I then tried to determine which part of the molecule of the drug was ~~the effective~~ responsible for its effects on the disease and concluded that it could well be the imidazole group present in Clet. For this reason I later tried the effects of various other substances containing this imidazole grouping & in particular the 5-nitroimidazoles ~~& found~~ on active RA - I found that these were equally effective to Clet- ~~& concluded~~ in their beneficial action in active RA - ~~& for this reason concluded that~~ These substances are well known antiprotozoal drugs. ~~& Such~~ The effects of these drugs

in cases of RA had never been prev. reported. (4.
For these reasons I concluded that ~~RA~~ RA must be
due to infection c̄ a pathogenic protozoon,

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a ~~Conclusion~~ Suggestion which has never previously been made.

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[~~The free living Amoeba prev. isolat~~ The 5 nitro-
imidazoles, like Clot before, were tested in the
laboratory against ~~the~~ cultures of the free-living
amoeba isolated from the tissues in cases of
active RA + found to kill the organisms. These
5 nitroimidazole included ~~both~~ metronidazole &
tinidazole. All this work was first reported in
my monograph entitled — — publ. by — — in
March 1978] Contrary to the suggestion of the
Examiner it was not known prior to my
disclosure in 1975 that Clot had an
antiprotozoal effect other than against Histoplasma
and while metronidazole + tinidazole are known
antiprotozoals, since no one had ever
demonstrated that RA might be due to a
protozoal infection, no persons had ever
suspected that they might have an

anti rheumatoid effect. In answer to (d) (5
the screening of antiprotozoal agents for use in
RA is not easy since ~~they~~ all chemical
substances containing an amide group tend
to cause an Herx reaction in this disease - this consists of
an exaggeration of the symptoms of the disease - When 1st
administered & results from the killing of
the causal organism in the tissues by the drug -
∴ of this the beneficial effect of these agents
is not immediately obvious until the Herx
reaction has died down - Hence ~~the~~ most
observers would ~~not have~~ conclude that they
were of no benefit = they had not waited
long enough to determine this - The occurrence of this reaction
alone proves the causative ~~not~~ relationship of
a protozoon to RA, an hitherto undescribed
finding - The whole of this argument can
be found in my 500 page monograph as
prev. mentioned above * I would point out
(that the Examiner's ~~has his~~ argo arguments

are back to front, — They assumed that the cause of RA was known to be a protozoan prior to my work — whereas until my work & antiprotozoal agents, it's nature had been completely unknown. —

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[Incidently in USA there have already been granted patents for the use of the above drugs in the treatment of RA. — of being the ~~newer~~ first person to describe their action in this disease —

16