Selection of pesticides to reduce human and environmental health risks: a global guideline and minimum pesticides list

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Summary

Background Pesticides present widespread risks to human and environmental health, yet selection criteria for end-users that factor in differences in risk between compounds are scant. We developed a system to classify pesticide risks and hazards with respect to human and environmental health and produce a minimum (lower risk) pesticide list.

Methods We classified 659 pesticides by acute and chronic risks to human health (eg, respiratory and carcinogenic effects) and by environmental risks, including biomagnification and atmospheric ozone depletion and risks to aquatic life, terrestrial wildlife, and pollinators. From this analysis, we produced a guideline for selection of lower risk pesticides. The classification of highly hazardous and high-risk compounds has been tested in more than a million farm households in the tropics, and in US integrated pest management (IPM) programmes. The full classification, including the minimum pesticide list, has been used in management of the fall armyworm (Spodoptera frugiperda) throughout Africa and Asia.

Findings Our analysis developed a stand-alone guideline for selection of lower risk pesticides. When classifying pesticides in current use against the fall armyworm in Africa, our guideline identified chemicals that are effective and of lower risk to human and environmental health. We argue that a minimum (lower risk) pesticides list, which meets IPM needs, could be developed from our classification system.

Interpretation As far as we are aware, our analysis is the first to propose a method for implementing the idea of a minimum pesticide list and the first to outline lower risk candidate compounds. Currently accepted criteria for defining highly hazardous pesticides do not adequately protect human bystanders, aquatic life, terrestrial wildlife, and pollinators.

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Introduction

Highly toxic pesticides are still in widespread use internationally and constitute a substantial challenge to human health.1–4 Evidence for the full extent of the global health burden associated with pesticide use is fragmentary, and scientific knowledge is scant regarding the extent of ecological disruption that pesticides cause and their fate and behaviour in the environment.5–8 However, evidence demonstrates the negative health and environmental effects of pesticides, and there is widespread understanding that intensive pesticide application can increase the vulnerability of agricultural systems to pest outbreaks and lock in continued reliance on their use.5–9 One of the major pathways for progress in limiting pesticide risks is the adoption of integrated pest management (IPM). IPM offers a framework for managing economic, health, and environmental risks while minimising undue outcomes for crop production: this was the guiding tenet of IPM when it was first envisioned.9 IPM adoption has led to sustainable reductions in the amounts of pesticides applied in intensively managed cropping systems in the USA and in smaller scale production in Africa and Asia.10,11 The failure to incorporate actionable information about pesticide effects as a part of IPM has, however, limited our capacity to reduce the human health and environmental risks posed by pesticides,12 a key goal of the International Code of Conduct on Pesticide Management.13 To resolve this shortfall, focus needs to be shifted beyond the regulatory processes that register pesticides on a case-by-case basis for use in agriculture onto education and market-based processes that encompass the whole system. These processes can limit risks associated with seasonal programmes of pesticide use, particularly in the developing world.13 To make progress, farmers and their advisors need access to science-based assessments of risks in a form that allows for risk-based comparisons between products.

We aimed to comprehensively analyse pesticide risks and produce a guide structured to enable decision making and serving to reduce negative effects on human health and the environment. We further aimed in our
Analysis to identify a lower risk group of pesticides by progressively filtering out compounds that are acutely toxic via dermal and inhalation exposure, pesticides that are carcinogenic, teratogenic, and mutagenic, and pesticides that require substantial levels of both training and personal protection to mitigate human health risks. We also filtered out pesticides that are toxic to aquatic life, terrestrial wildlife, and pollinators and compounds that magnify through food chains or deplete atmospheric ozone. With this approach, we aimed to distil a group that magnify through food chains or deplete atmospheric ozone and results in smallholder farmers, who do not have access to basic pesticide education, purchasing and using hazardous chemicals at high risk to themselves, their families, and the ecoclogical services on which farming depends. In The Lancet in 2002, Eddleston and colleagues called for a minimum (lower risk) pesticides list that could meet pest management needs with lower risk chemicals that have reduced potential for adverse effects. A partnership between Oregon State University, the Sustainable Agriculture Network, and the Rainforest Alliance made initial progress towards this goal, through identification of highly hazardous and high-risk pesticides from a list of more than 650 active ingredients. The resultant pesticide lists progressed through several stages of peer-review and have been effective in practice, reducing use of the most hazardous pesticides, guiding selection of lower risk pesticides, and mitigating risks to humans and wildlife in more than 50 countries.

Added value of this study
We have progressed further towards defining a minimum pesticides list by expanding our analysis to identify a large group of lower risk pesticides. We provide, for the first time, a scientifically based classification of most currently marketed pesticides, which can be used to support pest management decision making and guide the transition to lower risk chemicals and reduced adverse effects. We tested our pesticide classification system in Africa and Asia by selecting lower risk pesticides that could be used effectively against fall armyworm (Spodoptera frugiperda).

Implications of all the available evidence
The implications of this classification for pest management practice, pesticide regulatory policy, and research into both pesticide use and adverse effects are important. By testing the hazardous and high-risk pesticide classification system among at least a million farmers, we have shown the potential effect of this approach in reducing pesticide risks to human health and the environment on an international scale. By using the classification to select lower risk pesticides to use against fall armyworm in Africa, we highlight the value of this simple method in decision support. Importantly, we offer here the first candidate minimum pesticides list, which has the potential to meet most pest management needs while protecting and prioritising human and environmental health.
environmental or health risks; and lower risk pesticides more likely to be compatible with sustainable IPM. 13
In recognition of the limited access to education and resources in the developing world, we further subdivided the lower risk group, separating pesticides that require some specialised personal protection equipment (PPE), such as face masks or respirators, from those that need only baseline attire. 13
Since it was judged important to the practicality of our classification, we developed risk mitigation measures and criteria that could be applied to pesticides in the high-risk classification. We aggregated risk models associated with similar environmental compartments and developed mitigation measures that limited risks to aquatic life, terrestrial wildlife, pollinators, and human bystanders (appendix pp 24–27). These risk mitigation practices were based on validated best management practices and risk management requirements commonly used on the pesticide labels of more advanced regulatory jurisdictions.

The final stage of our process was to review and refine the lower risk pesticide list. This list consists of pesticides that did not meet the hazard classification or risk criteria that we used to assign pesticides to either the HHP category or the high-risk group. To refine this list to address requirements for PPE, we reviewed published risk assessments for every pesticide and assigned a level of PPE that would protect users during mixing, loading, application, and clean-up. This process accounts for uncertainties associated with pesticide use by untrained handlers and applicators in the developing world, since many handlers do not have access either to education about pesticide risks or to recommended PPE. 13

Redefinition of HHPs to include environmental and bystander health hazards
We based our categorisation of HHPs on the definition proposed by the JMPM in 2008. 14 The definition includes eight non-overlapping criteria that encompass acute and chronic toxicity, pesticides cited under international conventions, and pesticides that have shown evidence of widespread and severe human health or environmental effects.

For acute toxicity, we used the WHO class 1a and 1b hazard designation. 14 HHPs constitute the most acutely toxic compounds, typically by orders of magnitude when compared with other pesticides. For chronic toxicity, we used Globally Harmonized System of Classification and Labeling of Chemicals (GHS) criteria for carcinogenicity, mutagenicity, and reproductive toxicity. 14 The GHS system was set up to isolate pesticides and other chemicals that represent the highest levels of certainty related to adverse outcomes. By using the GHS 1a and 1b classification to designate pesticides as HHPs, the JMPM included pesticides with human or compelling animal evidence for carcinogenic, mutagenic, or reproductively toxic potential and pesticides with evidence of cancer in animals as an outcome. 14

Three additional HHP criteria incorporate pesticides listed under the Stockholm Convention (which identifies products with the potential to be both toxic and bioaccumulative), the Montreal Protocol (which identifies ozone-depleting chemicals), and the Rotterdam Convention (Annex III) list (which serves to increase communication about hazardous products by requiring previous informed consent for signatories to the convention when chemicals cross national borders). 14
Finally, through a process that we undertook with the Sustainable Agriculture Network, we added pesticides to our HHP classification that met criterion 8 of the JMPM definition, based on data from the Sustainable Agriculture Network that span more than 50 countries in the tropics. Criterion 8 addresses compounds associated with field evidence of severe human health or environmental effects; we recognise that pesticides listed under this criterion could vary by location and context. 14

Our analysis allowed us to examine whether currently defined HHPs are represented among the pesticides that pose the highest risks to aquatic life, terrestrial wildlife, pollinators, and human bystanders (ie, people, other than farm workers, pesticide handlers, or their families, who are exposed to pesticides by inhalation). Current HHP criteria do not explicitly address these risk categories. 14

We identified the ten most toxic pesticides associated with the risk models that we used, expressed as an application rate that would trigger a 10% or greater likelihood of an adverse effect. 15 The most toxic pesticides were drawn from a frequency distribution of these application rates for all the pesticides that we analysed. We also calculated the 5th percentile of this frequency distribution (units g/ha) for each risk model to portray the relative sensitivity of different environmental and human health endpoints. High representation of current HHPs among the ten most toxic pesticides for different risk models would suggest that existing criteria for HHP designation are also protective against important environmental and bystander risks. Low representation of existing HHPs within our analysis would suggest that HHP classification requires review and modification to account for these additional risks.

Analysis of current pesticide use against the fall armyworm
We applied our methodology to show its use in the context of pesticide application by smallholder farmers. We identified pesticides in current use in Africa against the fall armyworm and classified them using the information in our guideline. We assigned efficacy ratings (unknown, poor to fair [<70% to <80% control], and good-to-excellent [80–100% control]) based on field experiments and experience with fall armyworm management in the Americas and in Africa. From this categorisation, we isolated a list of both low risk and efficacious pesticides among those in current use by smallholder farmers.
Efficacy unknown

Poor-to-fair efficacy (<70% to <80% control)

Good-to-excellent efficacy (80-100% control)

Highly hazardous pesticides
Fipronil, methamidophos, monocrotophos, phorate
Carbofuran, carboxalil (obscure substance), dichlorvos, imidacloprid, thiamethoxam, trichlorphon
Beta-cyfluthrin, cyfluthrin, methomyl

High-risk pesticides to health and environment requiring maximum PPE with engineering and behavioural mitigations
Cartap hydrochloride
Abamectin, benfuracarb, carbaryl, chlorpyrifos, diazinon, dimethoate, fenothion, malathion, pirimiphos-methyl, profenofos, thiocarb
Acephate, gamma-cyhalothrin, lambda-cyhalothrin, cypermethrin, deltamethrin, diflubenzuron, emamectin benzoate, fenvalerate

High-risk pesticides to health and environment requiring double-layer PPE and either eye or respiratory protection, or both
Pyridalyl
Acetamiprid
Bifenthrin, alpha-cypermethrin, beta-cypermethrin, indoxacarb

Lower risk pesticides to health requiring single-layer PPE, but high environmental risk
Acetamiprid
Pyridalyl
Lufenuron, novaluron, spinetoram, spinosad, trihübzenuron, triflumuron

Lower risk pesticides to health and environment requiring single-layer PPE
Pyriproxifen
Bacillus thuringiensis serovar kurstaki, Beauveria bassiana, Metarhizium anisopliae
Azadirachta indica, Bacillus thuringiensis serovar aizawai, chlorantraniliprole, flubendiamide, methoxyfenozide, Spodoptera frugiperda nuclear polyhedrosis virus (SfNPV), pyrethrum

Pesticides are classified by hazard, requirement for risk mitigation, and efficacy against the pest using the procedure outlined in the risk management guideline (appendix). PPE and other mitigation requirements are defined in the appendix. Efficacy data are based on current data and are subject to change as experience increases. PPE=personal protective equipment.

Table 1: Pesticides in current use in Africa against fall armyworm (Spodoptera frugiperda)

Role of the funding source
The funders had no role in study design, data collection, data analysis, data interpretation, or writing of this report. PCJ had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results
Our stand-alone guideline for pest management decision makers is available in the appendix (pp 1–23). Of 659 pesticides assessed, 133 were assigned to the HHP classification, with an additional 25 classified as obsolete substances (appendix pp 7–11). 163 pesticides were classified as high risk and requiring mitigation of environmental and bystander health risks (appendix pp 11–15); this group also included compounds that would need higher level PPE (ie, double-layer clothing with face mask and respirator) to mitigate occupational health risks. Finally, we identified 95 pesticides that were of lower risk but would require additional PPE, such as face masks or respirators (appendix pp 15–17) and 243 pesticides of lower risk that would require only single-layer PPE (appendix pp 17–23).

In our analysis of pesticides in current use in Africa against the fall armyworm, we found that 13 pesticides were HHPs (one was an obsolete substance), 26 were high-risk pesticides requiring risk mitigation, and 17 were lower risk pesticides (table 1). Of the 11 lower risk compounds that only require single-layer PPE, at least seven had good-to-excellent efficacy against fall armyworm. The diversity of modes of action for these lower risk pesticides is such that selection pressure for resistance could be limited by rotating between them. Eight of 30 pesticides classified in our guideline as highly toxic to aquatic life (including aquatic algae, aquatic invertebrate, and fish reproduction) were current HHPs (table 2): 20 of these compounds had an aquatic risk mitigation requirement using our system (appendix pp 11–15). None of the compounds associated with algal risk were current HHPs, implying a lack of protection by the current HHP classification system for important aspects of aquatic ecosystem function.

Of 50 compounds classified in our guideline as toxic in the terrestrial environment, including risks to small mammals, birds (acute and reproductive), earthworms, and pollinators, 25 were categorised as HHPs (table 2). Four of these 25 compounds (three neonicotinoids and fipronil) were added to our current HHP classification under criterion 8 of the JMPM definition. A further 18 of the 50 toxic compounds had appropriate (terrestrial wildlife or pollinator) risk mitigation requirements in our guideline, but only one current HHP was represented among the ten most potent reproductive toxins for birds. Again, this finding implies scant protection for non-human vertebrates within the current HHP classification system.

Inhalation risk to humans was only represented by four current HHPs in our guideline, among ten of the most toxic pesticides to bystanders (table 2). This finding suggests a lack of protection to bystanders by existing HHP classification.

Pesticides with the largest number of risk mitigation requirements across multiple categories of risk were identified in our guideline. These compounds represent pesticides not classed as HHPs but having the broadest spectrum of activity. These pesticides are...
Discussion
Our comprehensive analysis of 659 pesticides represents a substantial expansion of pesticide risk information and decision support available in the public domain. Our guideline is intended to renew focus on the idea of a minimum (lower risk) pesticide list and to provide a practical means of planning for, and tracking, reduction of risks and pesticide effects at the farm scale and beyond.

Our classification system provides a means of transitioning from high-risk pesticides and HHPs towards lower risk pesticides and HHPs towards lower risk products when absolutely necessary. Use of this guideline will also provide a practical test of the minimum pesticide list idea, which could be used to limit pesticide effects on a global scale. This system is especially important in the context of smallholder pesticide use, providing an important decision-support tool that aims to protect vulnerable populations and the environment in areas where regulatory protections are lacking.

We have included both human health and environmental risks in our classification system for pesticides. By undertaking a comprehensive analysis of hundreds of compounds, we have subdivided most currently used pesticides on the basis of a common platform of risk criteria. Of particular note is the identification of a group of lower risk pesticides. Although human health risks alone would justify development of this lower risk classification, there are important environmental risks that can also be mitigated or reduced if pesticides are selected from this class.

Through our partnership with the Sustainable Agriculture Network, HHPs and risk management classifications presented here are currently in use on more than a million farms in the tropics (ie, at least 51 countries in Central and South America, Africa, and Asia). This system is also in use in Africa, as part of the response to the fall armyworm invasion, which affects smallholder maize farmers throughout the continent.

Table 2: Ranking of the ten most toxic pesticides in each risk model

<table>
<thead>
<tr>
<th>Aquatic algae (5th percentile) (g/ha)</th>
<th>Aquatic invertebrate</th>
<th>Fish chronic</th>
<th>Small mammal</th>
<th>Avian acute</th>
<th>Avian reproductive</th>
<th>Worm</th>
<th>Pollinator</th>
<th>Inhalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloropicrin</td>
<td>Gamma-cyhalothrin (A)</td>
<td>Gamma-cyhalothrin (A)</td>
<td>Aldicarb (HHP)</td>
<td>Terbufos (HHP)</td>
<td>Fenitrothion (HHP)</td>
<td>Sulfadoxin</td>
<td>1,3-dichloropropene (A, T, and P)</td>
<td>Cube extracts (B)</td>
</tr>
<tr>
<td>Azoxytrobin (A)</td>
<td>Bifenthrin (A)</td>
<td>Tefluthrin (HHP)</td>
<td>Terbufos (HHP)</td>
<td>Phorate (HHP)</td>
<td>Diquat dibromide (T and B)</td>
<td>Methyl isothiocyanate (A and B)</td>
<td>Imidacloprid (HHP)</td>
<td>Methyl isothiocyanate (A and B)</td>
</tr>
<tr>
<td>Oxyfluorofen (A and T)</td>
<td>Tefluthrin (HHP)</td>
<td>Tolfenpyrad (A)</td>
<td>Parathion (HHP)</td>
<td>Parathion (HHP)</td>
<td>Diquat ion (T)</td>
<td>Terbufos (HHP)</td>
<td>Clothianidin (HHP)</td>
<td>Terbufos (HHP)</td>
</tr>
<tr>
<td>Fentin hydroxide (A and T)</td>
<td>Methamidophos (HHP)</td>
<td>Lambda-cyhalothrin (A and P)</td>
<td>Oxamyl (HHP)</td>
<td>Aldicarb (HHP)</td>
<td>Dicofol (T and B)</td>
<td>Thiophonate-methyl (T)</td>
<td>Thiamethoxam (HHP)</td>
<td>Methyl bromide (HHP)</td>
</tr>
</tbody>
</table>

Letters next to each active ingredient indicate its status in our classification system. HHP-highly hazardous pesticide. A=aquatic risk mitigation. T=terrestrial risk mitigation. P=pollinator risk mitigation.
In the USA, the classifications we have presented (appendix pp 7–15) have been in use since 2016 in IPM extension programmes to farmers and other IPM practitioners. They have also been integrated within formal IPM strategic planning processes for several crops through which they inform pesticide regulatory decision making, reveal priorities for research and extension programmes, and provide a concrete tool for tracking progress in pesticide risk reduction.23

The table of lower risk pesticides in the appendix (pp 15–23) represents compounds that were distilled through our hazard classification and risk analysis procedures. This listing is important, but it is limited by the set of hazards and risks that we invoked in our process. Beyond the scope of our analysis, other risks might be known on a compound-by-compound basis, and end-users should consider this possibility before implementing the minimum pesticide list idea for specific applications. Additional risk factors that should be considered in further analyses include local products of choice for self-harm or suicide, contamination of natural resources (including surface water), or effects on biodiversity that result from scale of use or over-reliance on one compound.

Specific products also attract public controversy; included among such compounds is the herbicide glyphosate. Our analytical procedures placed glyphosate among lower risk pesticides, which aligns with the risk assessment procedures and conclusions of the JMPM that this compound is unlikely to be a carcinogen.24

New mechanisms are needed by which compounds that are toxic within the environment or to human health, but are not currently listed as HHPs, could be considered as candidates for global HHP classification. This step would broaden the HHP definition by the JMPM to account for effects of concern to important ecological services, in addition to human health, and promote adoption of regulatory, research, and education mechanisms to remove and replace these within the marketplace.25 We call on WHO and FAO to review approaches to HHP classification and the candidate compounds that we have listed. If the compounds we identified with the largest number of risk mitigation requirements were to be classified as HHPs then risks to humans via inhalation, risks to aquatic algae, and chronic reproductive effects on wildlife and the soil biota would be recognised formally in the definition of HHPs. We also suggest that pollinator effects should be included more formally among HHP criteria. The analyses that we have undertaken are based on fundamental properties and toxicological profiles and are intended for global application. Criterion 8 of the current JMPM definition of HHPs could still be used to address effects that apply to specific locations.

With respect to both human health and environmental risks, we have concerns about the scope and adequacy of current pesticide regulation internationally. The effects on human health of chronic long-term exposure to organophosphate, carbamate, and pyrethroid insecticides, for example, are not considered adequately by current regulatory risk assessment methods, with a call to eliminate some of these pesticides altogether from the marketplace.26 We provide here a mechanism to achieve reductions in risk, in advance of regulatory reform, through market-based and educational procedures that focus on lower-risk pesticides.

We know that pesticides have a role in biodiversity decline and that some materials are used on a very large scale, although the effect of their contribution relative to other drivers remains uncertain.26–27 Regulatory mechanisms are not currently set up to address biodiversity or ecological function as endpoints, although ecological considerations such as landscape structure and the capacity of species to recover are already known to interact with pesticide toxicity and persistence, to negatively affect natural enemies, aquatic life, and pollinators.28–30 Our guideline provides a mechanism to shift towards lower risk pesticides and limit environmental risks during a period when regulatory systems catch up with current scientific knowledge about pesticide effects.

The complex challenge of relying on regulation to limit pesticide effects that occur through mosaics of multiple compounds and uses that interact in space and time has led to assertions that we should act to curtail pesticide use overall.30 Our analysis is intended to contribute substantially towards this goal. Decision support for pesticide hazard and risk reduction can be incorporated within IPM programmes to reduce use of pesticides and the effects of these compounds while also managing pests. This process can and should take place regardless of the status of regulatory reform in a given context, but ideally it will complement gradually evolving regulatory mechanisms to deliver reductions in risk on a large scale.

The current system of classifying pesticides as HHPs should not be viewed as static or unchanging. We have access to new science, new tools, and new sources of evidence regarding effects, including those to the environment and human health (including self-harm).31 We also have new priorities for protection, such as pollination. The system should be adaptive enough to evolve in response to both needs and opportunities. Importantly, pesticide hazard and risk classification must be put into action within decision-support systems that inform farmers and other pest managers, rather than simply fueling the debate for and against pesticides.

We encourage more analyses that lead to real and measurable reductions in the risks and hazards associated with pesticide use. We also encourage publication of assessments of current pesticide use, particularly in developing countries, and publications identifying pest management priorities for farmers, extension agents, and regulatory authorities, so that important needs for pesticide hazard and risk reduction can be better understood and met, and progress tracked.21,23
Enough is known about pesticide health and environmental effects, and the inadequacy of relying on regulatory mechanisms alone, for action to be taken by educators, policy makers and others to limit use of pesticides while also protecting the ability to manage pests sustainably. We offer here a catalyst for progress and a candidate minimum pesticide list that could meet pesticide needs, particularly in the developing world.

Contributors
PCJ coordinated pesticide data sourcing and analysis and contributed to the literature search, table preparation, study design, interpretation of classification results, and writing of the narrative draft and associated guideline. PCJ also developed and analysed the highly hazardous pesticides (HHP) and risk mitigation tables (with the Sustainable Agriculture Network [SAN]), implemented the idea of the minimum pesticide list, developed the pollinator risk index and analytical regimen, contributed to development of risk mitigation procedures, developed the ideas for the lower risk pesticide classification and human health protection, and led the African case study. KM had the idea for this report, contributed to writing of this report, and is a primary reviewer of the guideline. KM also implemented the pesticide classification system within the Western Pesticide Risk Reduction Workgroup and within integrated pest management (IPM) strategic planning processes in the USA and Africa and contributed to interpretation of use of the system within IPM decision making and translation of the pesticide guideline for use within western USA and African IPM education. OB refined and developed the HHP classification and risk mitigation procedures, designed the public consultation for HHP and risk mitigation analyses, and contributed to stakeholder reviews of these classifications, the ideas for mitigation, and data collection and analysis for public consultations and stakeholder reviews. OB also contributed to writing of the draft risk mitigation criteria, interpretation of stakeholder input to HHP and risk mitigation lists, the final review of the HHP and risk mitigation analyses, and writing of the guideline. MAB implemented and documented the public consultation for HHP and risk mitigation classification within SAN and contributed to the stakeholder review of the HHP and risk mitigation classification systems. MAB also contributed to data collection and stewardship of the public consultations and stakeholder reviews of HHP and risk mitigation lists, analysis and interpretation of review data, data review of narrative and supplementary materials, and writing of this report and the guideline. LN contributed to the stakeholder review of the HHP and risk mitigation classifications, reviewed and collated information on the HHP status of pesticides, analysed and interpreted stakeholder review data, and reviewed the narrative and supplementary materials, including the classification status of all pesticides. LN also contributed to writing of this report and the guideline.

Declaration of interests
We declare no competing interests.

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